Chapter 2

Synthesis of novel atropisomeric *ortho*-substituted *ortho*-terphenyls

2.1 Introduction

Although atropisomers can be interconverted by rotation around single bond, the barrier of rotation is enough to prevent ready interconversion at ambient temperature and allow the isolation of individual stereoisomers.[1] An overview to this phenomenon is given in the introduction chapter. Terphenyls are aromatic hydrocarbons consisting of a chain of three benzene rings, Ar-Ar-Ar. These type of molecule have defined group of molecular triads **B-A-B** in which the central unit **A** is planar.

In this molecular triad **B-A-B**, the central unit **A** is planar (aromatic or hetero aromatic) and the component **B** can be achiral or chiral (not symmetrical with respect to the **A** component) and **A-B** link constitutes either a single bond, usually with restricted rotation or a flexible ring condensed to **A** and **B** parts. Non-coplanarity of **A** and **B** renders *syn* and *anti* stereoisomers. Figure 1 illustrates the different type of triads B-A-B.

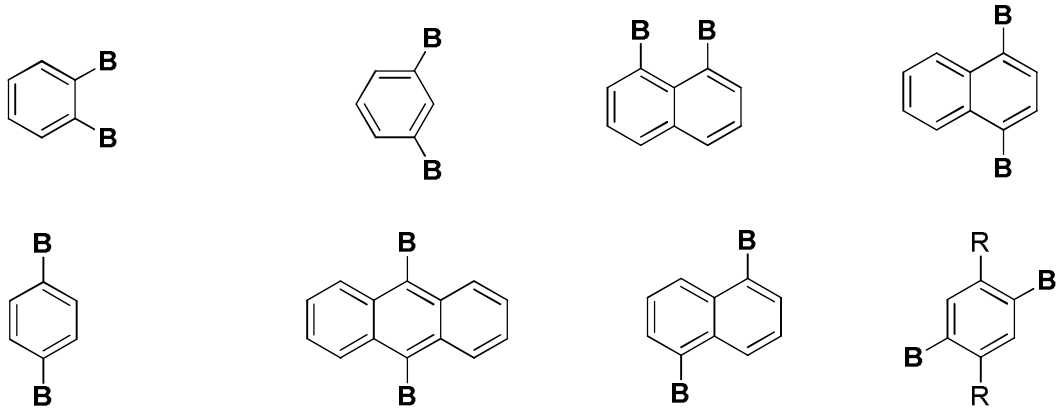
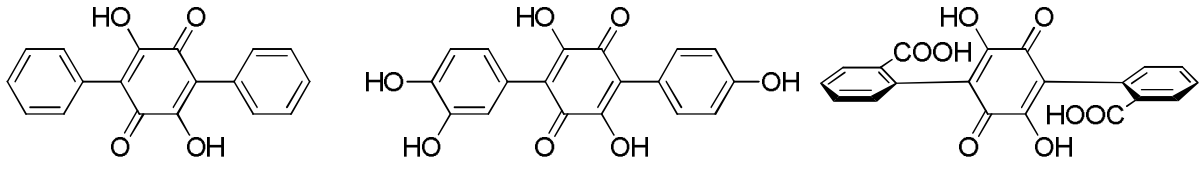


Figure 1

Very few terphenyl derivatives are reported as naturally occurring compounds. The most well known derivatives are polyhydroxylquinones.[2-5]



Polyporic acid Leucomelone Muscarufin

Figure 2: Naturally occurring terphenyls.

Nomenclature of Terphenyl

The two stereoisomers of the triad **B-A-B** are commonly labeled *syn* and *anti* or *C*-shaped and *S*-shaped. In the *syn* isomer both the molecule **B** are located over the same face of the **A** molecule and in opposite faces for *anti* isomer. However, in the projection demonstrating *C* or *S* shape the **B-A-B** molecule is viewed with the planar central unit **A** oriented perpendicularly to the plane of the drawing. This *syn* and *anti* prefixes used is generally accepted as stretreochemical descriptors,[6-8] it has not yet been officially recommended by the IUPAC Commissionon Nomenclature. Commonly C and S label is used to describe the two isomers of atropisomers.[9-11]

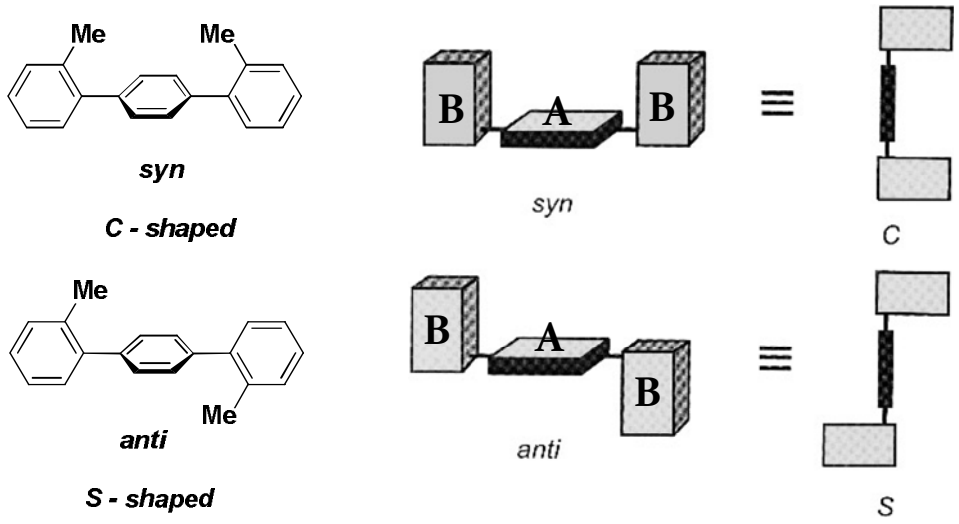


Figure 3: *syn* (*C*-shaped) and *anti* (*S*-shaped) conformers of the **B-A-B** triad.

The terphenyls are generalized as Ar-Ar-Ar where the two terminal aryl groups could be 1,2-fused or 1,3-fused or 1,4-fused on the central aromatic ring (Figure 4).

Types of terphenyls

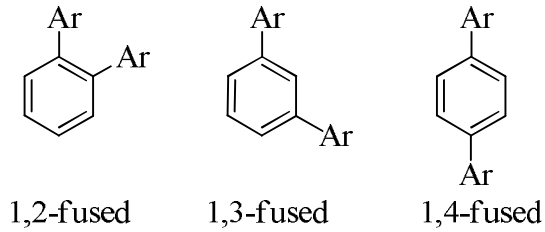


Figure 4

When the aromatic derivative bears two benzene rings in the *para*, *meta* or *ortho* positions as in 1,4 and 1,3 and 1,2 positions respectively, it leads to two atropisomers, with the two aromatic substituents in a *syn* or *anti* relationship. In the case of the *para* and *meta* derivatives the *syn* and *anti* isomers could not be isolable at ambient temperature but were detected by NMR spectroscopy.[12-17] In the more hindered 1,2 *ortho* fused derivative, the separation of the *syn* and *anti* atropisomers is possible at ambient temperature.[12,13]

Lunazzi and co-authors studied the conformational behaviour of 1,2- fused, 1,3-fused and 1,4-fused aromatic terphenyl derivatives.[18] They have also reported that the benzene ring bears two 2-methyl-1-naphthyl moieties in the *para*, *meta* or *ortho* positions such as in 1,4-bis(2-methyl-1-naphthyl)benzene **1**, 1,3-bis(2-methyl-1-naphthyl)benzene, **2** and 1,2-bis(2-methyl-1-naphthyl)benzene **3**. Due to the two naphthyl substituents oriented in *syn* or *anti* conformation, two rotational isomers (atropisomers) are generated. Extension of this system is in its tri-substituted analogue **4**. In order to establish their prediction, derivatives **1–4** were synthesized and the related stereomutation processes occurring in solution and in the solid state were investigated by NMR spectroscopy techniques (Figure 5).

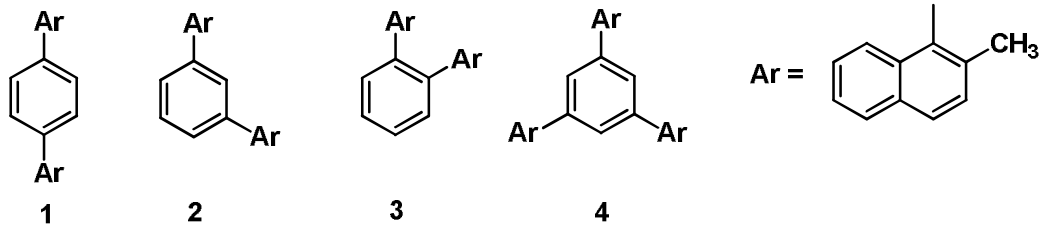


Figure 5

A considerable number of examples of the terphenyls involve *ortho*-substituted benzene derivatives and substantial efforts have been directed to the isolation of *syn* and *anti* conformers and/or the studies of their rotational barriers of interconversion. The presence of methyl groups in the *ortho-ortho'*-positions, as in **5,** is believed to be sufficient to hinder free rotation in biphenyl systems.[19] Mitchell *et al.*[20] reported the existence of *syn* and *anti* isomers of 2,2'-dimethyl-*o*-terphenyl **6** as apparent from the ^{1}H-NMR studies with a barrier to rotation ($\Delta \mathbf{G}^{\ddagger}$) of 62 kJ mol^{-1}[**6a** ↔ **6b**]. Roberts *et al.*[21] however, have reported the successful separation of the *syn* and *anti* isomers of 1,8-di-*o*-tolylnaphthalene **(7a** and **7b)** with an observed ($\Delta \mathbf{G}^{\ddagger}$) for rotation [**7a** ↔ **7b**] of 101 kJ mol^{-1}, although the

half-life with respect to interconversion in solution is about one day at room temperature. Lai and co-authors[22] reported the synthesis of both 9,l0-di-*o*- and 9,l0-di-*m*-tolylphenanthrene. The existence of the *syn* and *anti* isomers of the former is apparent from H-NMR data and one of the isomers was obtained in pure form by fractional crystallization. Conformational studies have revealed exceptionally high barriers of rotation ($\Delta \mathbf{G}^{\ddagger}$> 155 kJ mol^{-1}) for the aryl rings in 9,l0-di-*o*-tolylphenanthrene **8**. At room temperature, restricted free rotation of the aryl rings was also observed in 9,l0-di-*m*-tolylphenanthrene **9** ($\Delta \mathbf{G}^{\ddagger}$ 85 kJ mol^{-1}).

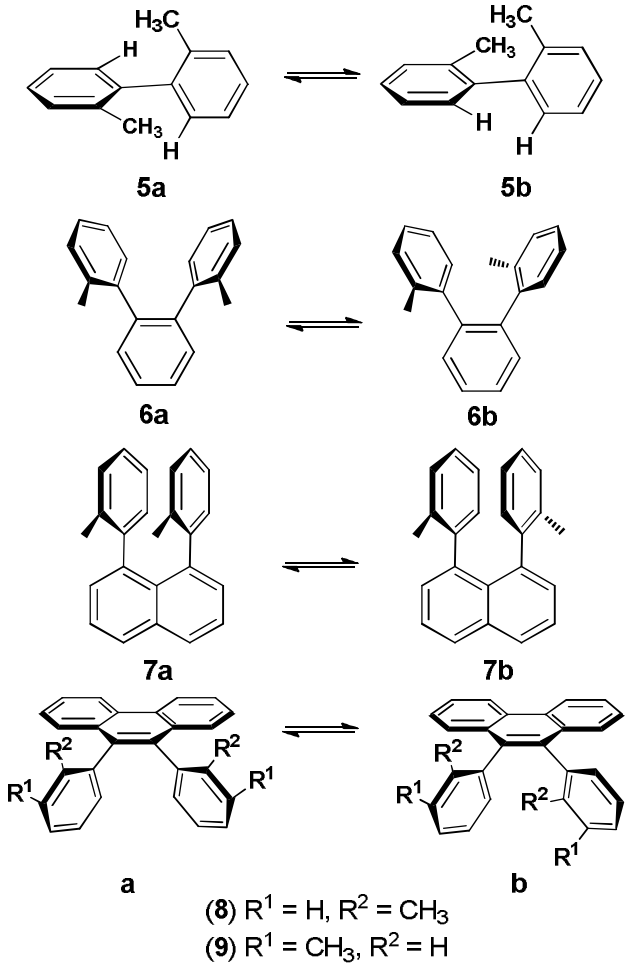


Figure 6

Roussel and co-authors reported bis-(N-aryl) atropisomeric triads.[23] In this work, a series of 1,2-bis-[4-methyl-2-(thi)oxo-2,3-dihydrothiazol-3-yl]-benzene compounds have been prepared. These atropisomeric molecular triads were exclusively found to exist in the *anti*-form. They were separated into enantiomers by liquid chromatography on a chiral support.

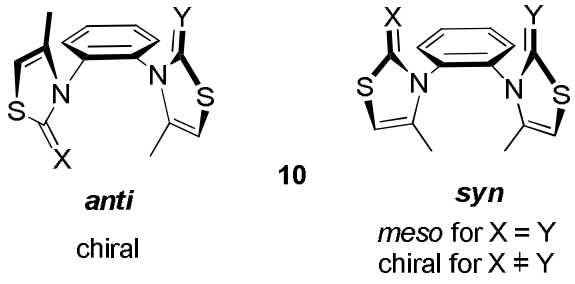


Figure 7: *anti* and *syn* forms of 1,2-bis-thiazoline-(thi)-one benzene

Apart from 1,2-*ortho* fused aromatic benzene substituted derivatives, 1,2-diaryltetrahydropyrimidine compound were synthesised and their conformational and stereodynamic properties were investigated by Mazzanti.[24] In order to verify effect of ring size, 1-(2-nitrophenyl)-2-(2-methylphenyl)-1,4,5,6-tetrahydropyrimidine and its five- and seven membered ring analogs were synthesized and their conformational properties investigated by low temperature NMR spectroscopy and DFT theoretical calculations.

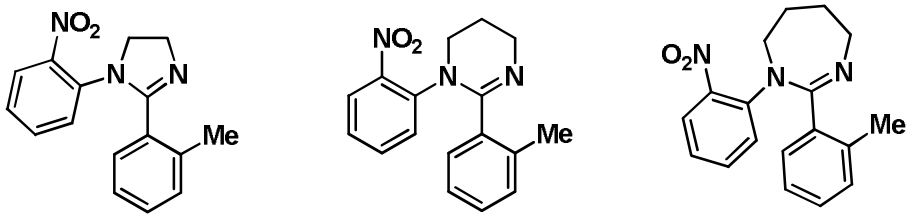


Figure 8

In a study of atropisomeric molecular triad of the B-A-B type, several issues have to be addressed.[25-54]

1. The occurrence of *syn*- (parallel) and *anti*- (antiparallel) forms. In the case of B-A-B triad the *syn*-form is a *meso*-form, whereas the *anti*-form is composed of a pair of enantiomers. In the case of B-A-B′ triad, both the *syn* and *anti* forms are composed of enantiomeric pairs (Figure 7).
2. The barriers to rotation about the two axes. The determination of the barriers is a key issue since it will impose the method of study, that is, DNMR, DHPLC, or chromatography on chiral support.
3. The resolution of the enantiomers and their absolute configuration. If the barriers are high enough to give stable atropisomers at room temperature, the method for the resolution of the enantiomers and the absolute configuration of each of them should be provided.

2.2 *Results and Discussion*

In this chapter, we have directed our interest to the 1,2 fused *ortho* substituted *ortho* terphenyls as a representative example. Without substitution on the terphenyl the bond rotation of the Ar-Ar bond is very rapid. Hence if the substitution is introduced at the appropriate site as in Figure 9, the steric crowding caused should be sufficient to prevent the rotation of Ar-Ar axis. Similar studies were carried out by Mitchell and co-workers who first synthesized 2,2'-dimethyl-*o*-terphenyl **6**. However the two isomers could not be separated due to low rotational energy barrier as was apparent from the NMR studies. Therefore our idea was to further introduce bulkier substituents on the methyl group to facilitate the separation of isomers.

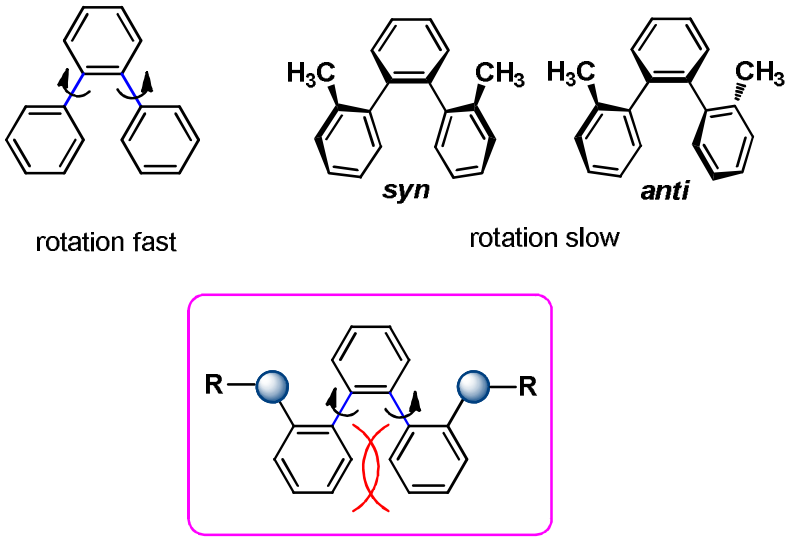
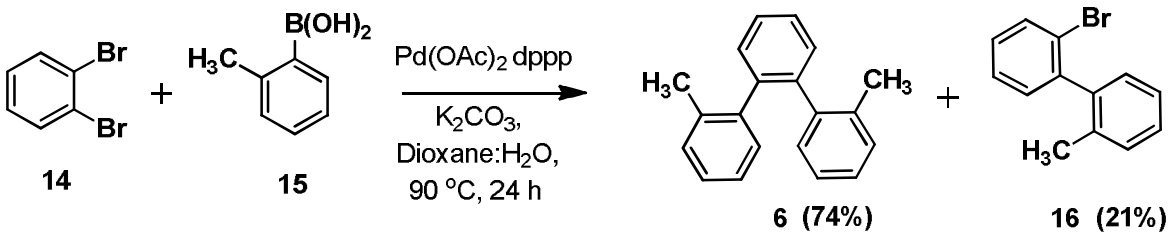


Figure 9

This Chapter is divided into two sections. In first section we present the synthesis of a series of *ortho*-substituted 1,2-terphenyl compounds. It was observed that all compounds showed conformational behaviour at room temperature as observed from the ^{1}H-NMR and we have also attempted resolution of these conformational isomers. In the next section the barrier of rotation for all synthesized compounds was measured by analyzing the variable temperature NMR spectra. Thermodynamic data and barrier of rotation for all the *ortho* terphenyl derivatives will be summarized.

2.2.1 Synthesis and resolution of *ortho* terphenyl derivatives

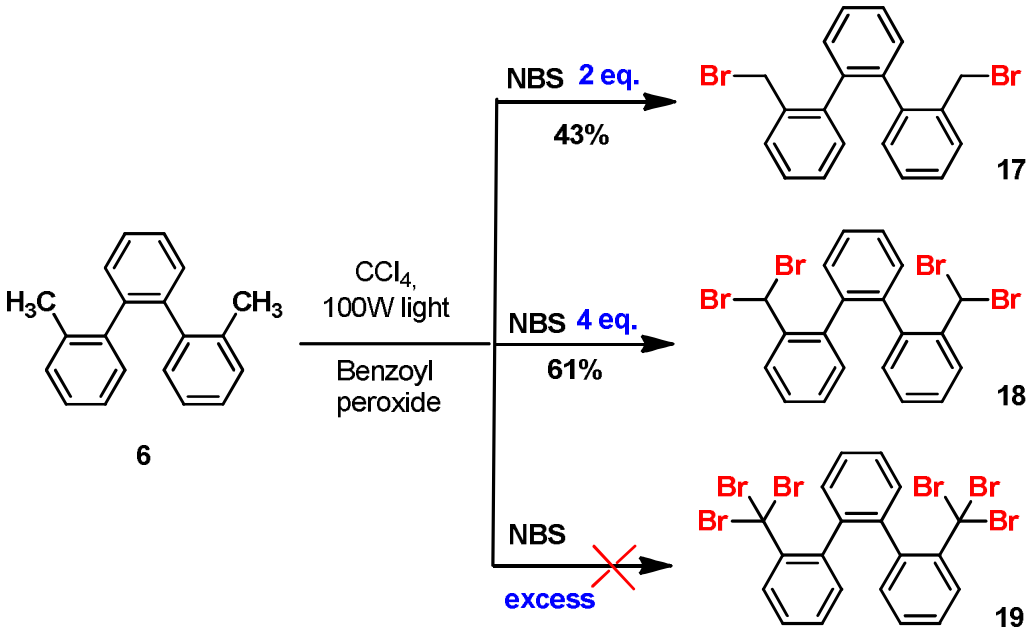
Mitchell and co-workers first synthesized the 2,2"-dimethyl-*o*-terphenyl **6** and they could not separate the isomers due to low energy barrier.[55] The synthesis of 2,2"-dimethyl-*o*-terphenyl derivatives and its study was undertaken by us.We began the synthesis of 2,2"-dimethyl-*o*-terphenyl with Suzuki reaction of 1,2-dibromo benzene **14** with tolylboronic acid **15** in the presence of Pd-dppp which furnished a mixture of terphenyl **6** along with the mono product **16**. It is interesting to note the presence of two slightly broad singlet signals for the methyl groups in **6**, probably indicating the presence of two atropisomers. The ratio of the two singlet signals is almost identical indicative that the isomers could be present in equal ratio.



Scheme 1

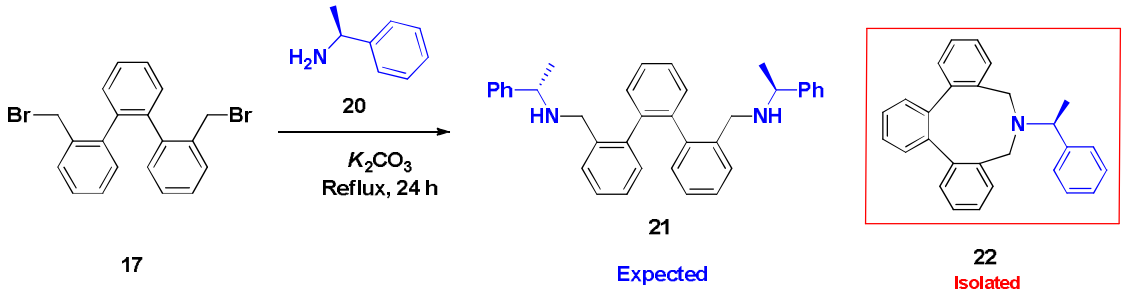
In order to restrict the C-C bond rotation in **6** we subsequently introduced the bulky bromine atom on the *ortho* position by side chain bromination. The bromination was carried out with *N*-Bromosuccinimide (NBS) on **6** by standard condition. The 2,2"-dimethyl-*o*-terphenyl **6** was converted to its dibromoderivative with NBS (2 eq.) giving 2,2"-bis(bromomethyl)-*o*-terphenyl **17**, and with 4eq./excess of NBS giving 2,2"-bis(dibromomethyl)-*o*-terphenyl **18**. However when we tried to introduce three bromine atoms at *ortho* position we could not succeed due to the bulky substituted bromine atom which increases crowding at *ortho* position and hence product **19** was not formed. The ^{1}H-NMR spectrum of 2,2"-bis(bromomethyl)-*o*-terphenyl **17** clearly showed an AB splitting pattern for the Ar-C*H*$_2$-Br protons, and showed two sets of signals at δ 4.2 ppm for mixture of *syn* and *anti* isomers with the ratio 63:37 irrespective of the order. Similarly for 2,2"-bis(dibromomethyl)-*o*-terphenyl **18** Ar-C*H*-Br$_2$ proton appeared as a singlet which

shifted further downfield (δ 6.67 ppm) and it has mixture of *syn* and *anti* isomers with the ratio 94:6.



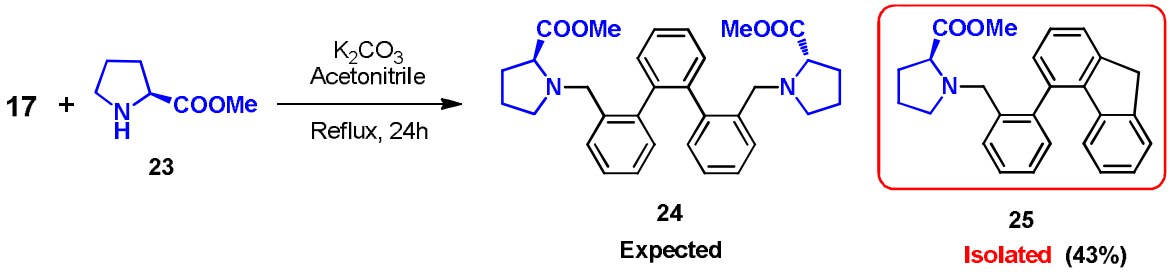
Scheme 2

The ^{1}H-NMR results of 2,2"-bis(bromomethyl)-*o*-terphenyl **17** encouraged us to resolve *syn* and *anti* isomers. Initially we tried to separate both *syn* and *anti* isomers through column chromatography but were unsuccessful. Then the 2,2"-bis(bromomethyl)-*o*-terphenyl **17** was treated with chiral 1^o amine, alpha-methyl benzyl amine **20** to make dialkylated diastereomeric molecule **21**, which can be easily separated by column chromatography or crystallization. However, we were unable to prepare the desired compound and a product of intramolecular cyclic dialkylation product **22** was obtained. The mass spectral analysis was in agreement with the structure of cyclic product **22**, with the molecular ion peak at 375 *m/z* as a base peak. The ^{1}H-NMR spectrum clearly showed broadening of the signal for the Ar-CH_2-N protons. The broad signal may indicate presence of a mixture of *syn* and *anti* isomers, mean while the methyl (-CH_3) protons also showed broad signals with same ratio of *syn* and *anti* isomers at ambient temperature in $CDCl_3$.



Scheme 3

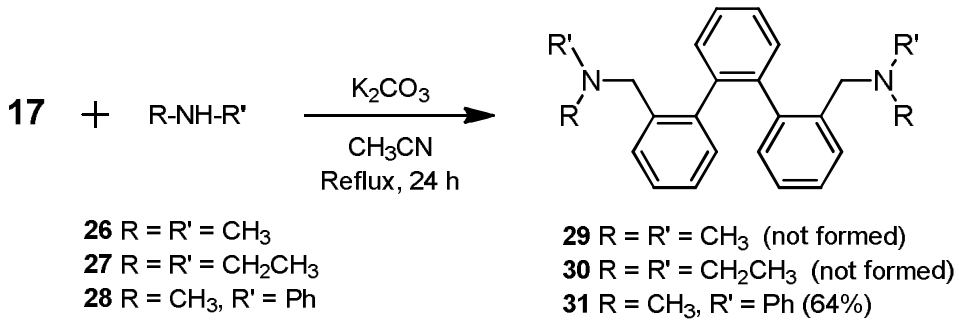
Again, we tried same reaction with (*S*)-methyl pyrrolidine-2-carboxylate **23** (2° chiral amine) in the presence of base. In this reaction we isolated the unexpected product **25**. The product was confirmed by spectral analysis. The ^{1}H-NMR spectrum showed -$COOCH_3$ ester signal as a singlet at δ 3.67, Ar-CH_2N methylene protons at 3.37 and 2.96, Ar-CH_2Ar protons appear as doublet at δ 3.42, chiral carbon proton (C*H*) appear as triplet at δ 3.25, rest of protons signal appeared at aliphatic region and aromatic protons (12H) appeared between δ 7.37-6.89 ppm region. The mass spectrum showed molecular ion peak at 383 *m/z* and after fragmentation of –$COOCH_3$ 324 *m/z* and -NC_4H_7 255 *m/z*.



Scheme 4

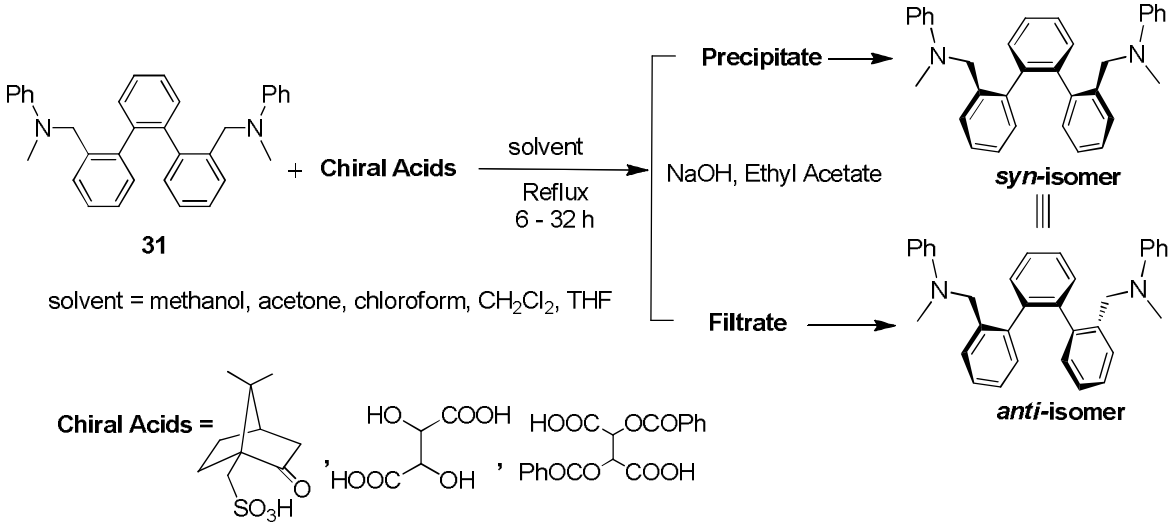
In continuation next the 2,2"-bis(bromomethyl)-*o*-terphenyl **17** was treated with aliphatic 2° amine (dimethyl amine **26** or diethyl amine **27**) in the presence of base, however, the reaction resulted in complex products and no significant quantity of single compound was isolated. Hence, other secondary amine *N*-methyl aniline **28** was used in the same condition and the desired product **31** was isolated as a white solid with 64% yield (Scheme 5). The product was characterized by spectroscopic analysis. The ^{1}H-NMR spectrum clearly showed an AB splitting pattern for the Ar-C*H*$_2$-N protons, and appeared two sets of signals for mixture of *syn* (4.57 & 4.11) and *anti* (4.24 & 4.12), likewise the methyl protons also showed two sets of signals with same ratio of *syn* (2.85) and *anti* (2.77) isomers at ambient temperature in $CDCl_3$. The high resolution mass spectrum showed the

molecular mass of the product and its isotope pattern were consistent with the calculated value for $C_{34}H_{32}N_2$ $[M + 1]^+$ 469.2644, found 469.2638 *m/z*.



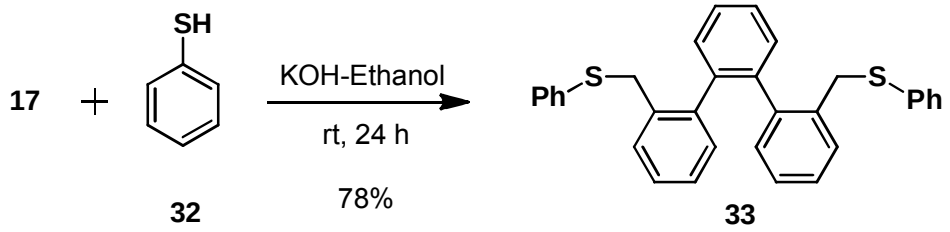
Scheme 5

The separation of *syn* and *anti* isomers of compound **31** can be carried out by diastereomeric salt formation method using chiral acids, for that purpose we tried nitrogen contained compound **31** crystallized with different chiral acids such as camphor sulphonic acid, tartaric acid and dibenzoyl tartaric acid in different conditions (Scheme 6). In all case we could not separate the two isomers.



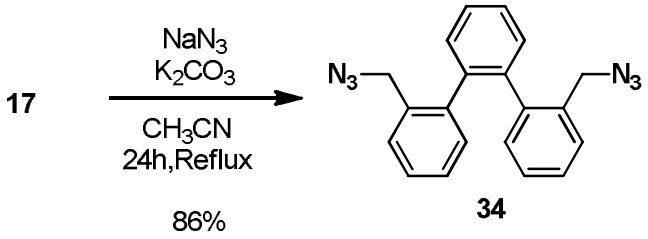
Scheme 6

In order to study the effect of functional groups on Ar-Ar bond rotation, the dibromo **17** was converted to various functional groups. The 2,2"-bis(bromomethyl)-*o*-terphenyl **17** was transformed to 2,2"-bis((phenylthio)methyl)-*o*-terphenyl **33** by simple methanolic KOH using benzenethiol **32** (Scheme 7).



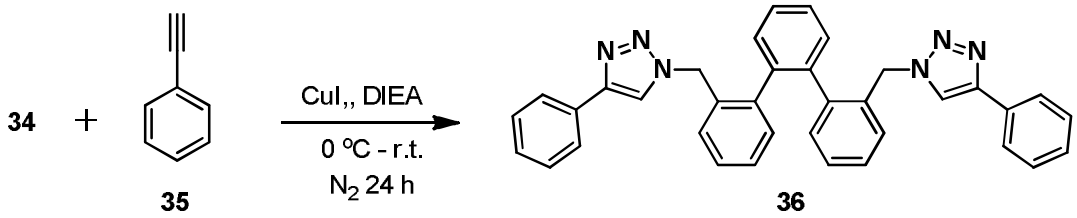
Scheme 7

The 2,2"-bis(bromomethyl)-*o*-terphenyl **17** was then converted to the 2,2"-bis(azidomethyl)-*o*-terphenyl **34** by simply heating with sodium azide (Scheme 8). the IR spectrum showed azide (N_3) stretching at 2120 cm^{-1}, the mass spectrum agreed with molecular ion peak 340 *m/z,* and the ^{1}H-NMR spectrum of **34** the Ar-CH_2-N_3 part is showed AB splitting pattern clearly, and shows that *syn* and *anti* isomers with ratio 60:40.



Scheme 8

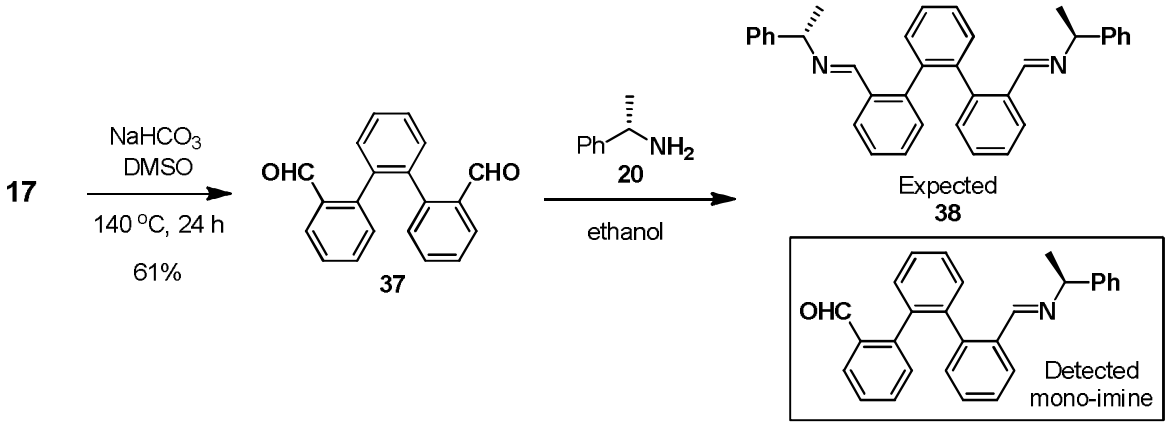
The 2,2"-bis((4-phenyl-1H-1,2,3-triazol-1-yl)methyl)-*o*-terphenyl **36** was prepared by simple click chemistry with phenyl acetylene **35** (Scheme 9). The product was confirmed by spectral analysis. The ^{1}H-NMR spectrum of **36** also showed AB splitting pattern for Ar-CH_2-N methylene protons and *syn* and *anti* isomers ratio was tentatively assigned to be 38:62. The high resolution mass spectrum showed the molecular mass of the product and its isotope pattern were consistent with the calculated value for **36** $C_{36}H_{28}N_6$ $[M + Na]^+$ 567.2273, found 567.2266 *m/z.*



Scheme 9

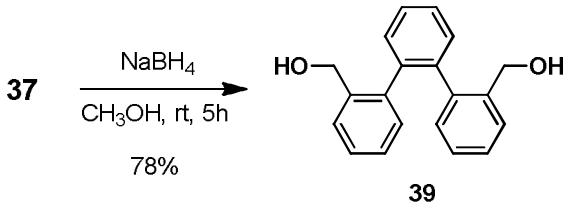
The ^{1}H-NMR of **31**, **33** and **36** clearly showed two sets of signal for *syn* and *anti* isomers. For the separation of isomers, initially we tried column chromatography, then making diastereomeric salt formation. Further in order to separate the two isomers we tried to derivatize compound **17** into its bulkier homolog. For that **17** was converted to the 2,2"-

diformyl-*o*-terphenyl **37** by Kornblum oxidation (Scheme 10), which was then treated with chiral 1^{o} amine **20** with an intension of making diastereomeric bis-imine **38**. However, we failed to convert both aldehydes to the bis-imine **38** (Scheme 10) and the mono imine was detected by ^{1}H-NMR spectrum, and mass showed 389 m/z molecular ion peak, after fragmentation of -2H gives 387 m/z as a base peak. The ^{1}H-NMR of **37** showed two singlet signals for aldehyde proton at δ 9.85 and 9.79 which was corresponding to *syn* and *anti* isomers. The Mass spectrum (EI) showed molecular ion peak at 286 *m/z*. The IR spectrum showed aldehyde (-CHO) stretching frequency at 1692 cm.$^{-1}$



Scheme 10

Then 2,2"-dicarbaldehyde-*o*-terphenyl **37** was converted to *ortho*-terphenyl-2,2"-diyldimethanol **39** by reduction using sodium borohydride (Scheme 11). The ^{1}H-NMR showed broad AB splitting signal for Ar$\underline{CH_2}$OH protons, EI–Mass showed molecular ion peak [M+1], which on fragmentation of $-H_2O$ give 273 *m/z* as a base peak. The IR spectrum showed -OH stretching frequency at 3345 cm^{-1}. Attempts of enzymatic resolution of compound **39** by kinetic resolution using lipage and vinyl acetate were not successful.



Scheme 11

As evident from the foregoing discussion, it is clear that separation of *syn* and *anti* isomers not possible, probably due to lower barrier to rotation at room temperature. In next section we have measured the barriers of rotation of all synthesized compounds by dynamic ^{1}H-NMR analysis.

2.2.2 Characterization and dynamic NMR study of *ortho*-terphenyls

The structures of the *ortho*-substituted-*o*-terphenyl and derivatives synthesized were determined by spectroscopic analysis (IR, ^{1}H and ^{13}C-NMR), mass spectrometry including high resolution mass, and in one case, by single crystal X-ray diffraction analysis.

Stereochemical Properties of *ortho*-Terphenyls

All compounds belong to the family of *ortho*-terphenyls. Conformational analysis of *ortho*-terphenyl derivatives have been described as illustrated in Figures 10 and 11.[56] These type of compounds show two basic average conformations, chiral *anti* and achiral *syn*, depending on the mutual orientations of the largest R substituents with respect to the plane of the central phenyl fragment. Exchange between these forms results from rotation about the phenyl–phenyl (Ar–Ar) bonds. In addition, oscillation motions determine limiting forms, which are enantiomeric and degenerate in the case of the *syn* conformation, and diastereomeric in the case of the *anti* conformation, that is, *anti-in* and *anti-out*, depending on the position of the R substituent with respect to the C_2 symmetry axis of the molecule: remote (*out*) or close (*in*).

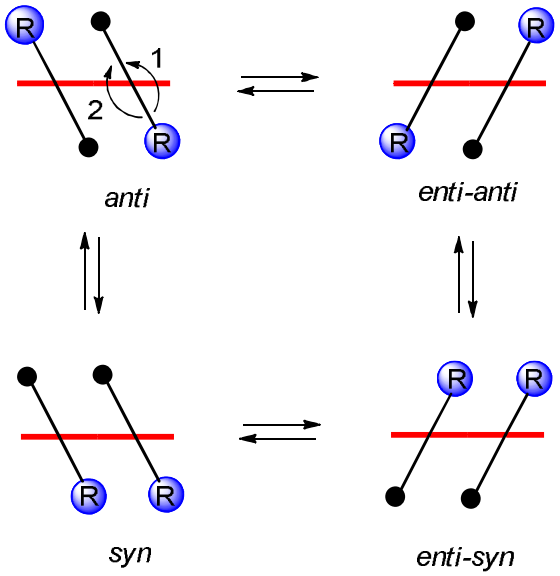


Figure 10:The *anti* and *syn*conformations of *ortho*-terphenyls. The blue disk represents the largest R substituent. Curved arrows represent the two possible pathways for the *anti*/*syn* interconversion.

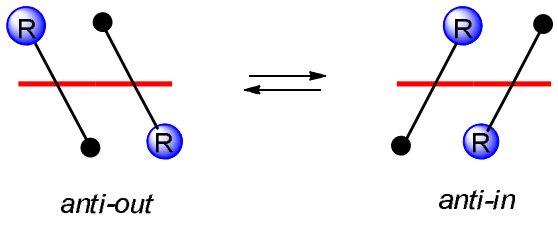


Figure 11: The *anti-in* and *anti-out* conformations of *ortho*-terphenyls. The blue disk represents the largest R substituent.

Variable temperature NMR study of terphenyls derivatives

The room-temperature ^{1}H-NMR spectra of **6**, **17**, **18, 31**,**33**, **34**, **36**, **37** and **39** display well resolved features, for *syn* and *anti* isomers which can be clearly distinguished at ambient conditions.

An interesting aspect of the ^{1}H-NMR spectrum of 2,2"-dimethyl-*o*-terphenyl **6** is that it shows two slightly broad singlet signal for the methyl group in $CDCl_3$ at δ 2.13 & 2.05 ppm at room temperature. The two isomers *syn* and *anti* could not be isolated on column chromatography. This could be because of low energy barrier, and rapid interconversion of the two isomers at ambient temperature. This atropisomerism can be well comprehended using Variable-temperature (VT) ^{1}H-NMR spectroscopic studies. From the VT-NMR studies for **6** in $CDCl_3$, it is observed that the methyl signal coalesce near to 35 ^oC as seen in the stacked plot in the Figure 12A. When the temperature increases, *syn* isomer is converted to *anti* isomer. Hence with this purpose, when we recorded ^{1}H-NMR at 40 ^oC, the methyl signal gave sharp singlet and we kept this sample for 10 minutes at this temperature. On further recording the ^{1}H-NMR, there was no change in the signal. Then gradually, on cooling the same sample the methyl signal reappears into two signals with the same ratio. This indicates that *syn* and *anti* isomers can exhibit rapid interconversion of the two conformers at high temperature. Structurally similarly type of compound 2,2"-dicarbaldehyde-*o*-terphenyl **37** showed *syn* and *anti* mixture in $CDCl_3$ representing the signals at δ 9.948 and 9.798 ppm for the aldehyde proton (C*H*O). In the VT-NMR studies for **37** in DMSO-d_6 the aldehyde proton signal broadens and coalesces, finally yielding a single line, owing to the rapid interconversion of the two conformers at high temperature (Figure-12B). On cooling the signal broadens and reappears as two signals at room temperature, The rate constants for this process was determined and from coalescence temperature (*T*c) method,[57] the corresponding free energy of activation ($\Delta G^{\ddagger}$ 71.05 kJ/mol, as in Table 1) was derived.

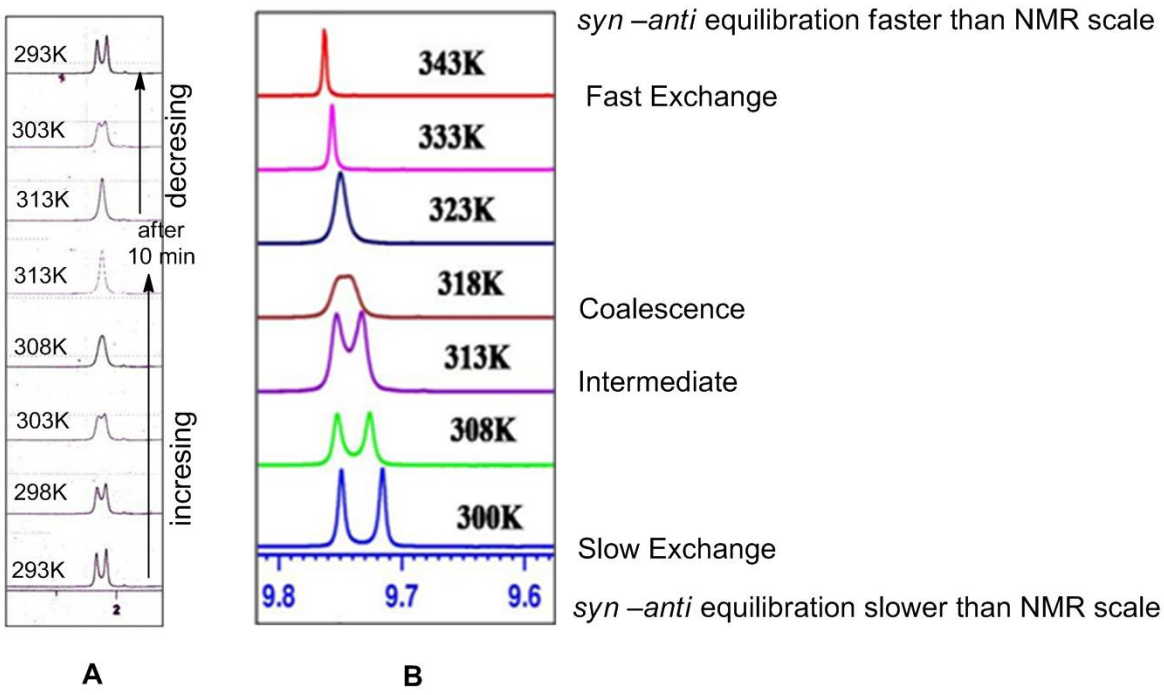


Figure 12: A). Stacked plot of the VT ^{1}H NMR spectra of terphenyl **6** (Ar-**CH$_3$** region). B). Stacked plot of the VT ^{1}H NMR spectra of terphenyl **37** (Ar-**CHO** region).

In order to identify the NMR signals of each isomer, we tentatively assigned the ^{1}H-NMR signals in 2,2''-bis(bromomethyl)-*o*-terphenyl **17,** the *anti* isomer of methylene protons are more shielded since they appear below the other aromatic ring. Variable-temperature (VT) H-NMR spectroscopic studies provide more interesting information on this atropisomerism. On raising the temperature of a $CDCl_3$ or DMSO-d_6 solution of **18**, the NMR methylene (-CH_2Br) protons of the *syn* isomer and of the *anti* isomer broaden even at 52 ^{o}C in $CDCl_3$, and at 80 ^{o}C in DMSO-d_6 (Figure 13), eventually we could not get coalesce, as well as a single line, due to the limitation of the boiling point of $CDCl_3$, but in the case DMSO-d_6 the analysis was carried out up to 353K. During the analysis we observed that with increasing the temperature the methylene protons were broaden at 333K, and on further heating (increased by 10 ^{o}C) the methylene proton signals disappeared at 343K as shown in Figure 13.

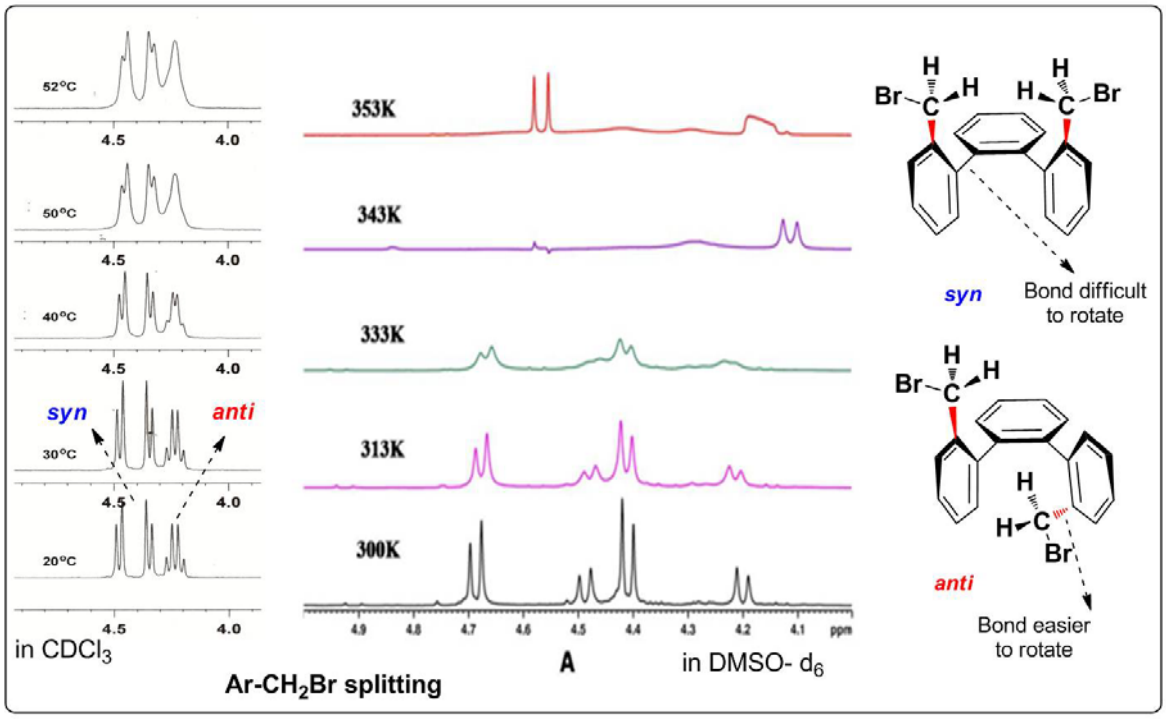


Figure 13: Stacked plot of the VT ^{1}H-NMR spectra of terphenyl **17** (Ar-**CH_2**-Br region)

On raising the temperature of a DMSO solution of **18**, the NMR methylene (CH) singlet of the *syn* isomer and of the *anti* isomer broaden and coalesce, eventually yielding a single line, owing to the rapid interconversion of the two conformers at high temperature (Figure 14). From coalescence temperature (T_c) method, the free-activation energy was derived ($\Delta G^{\ddagger}$ 84.36 kJ/mol, as in Table 1).

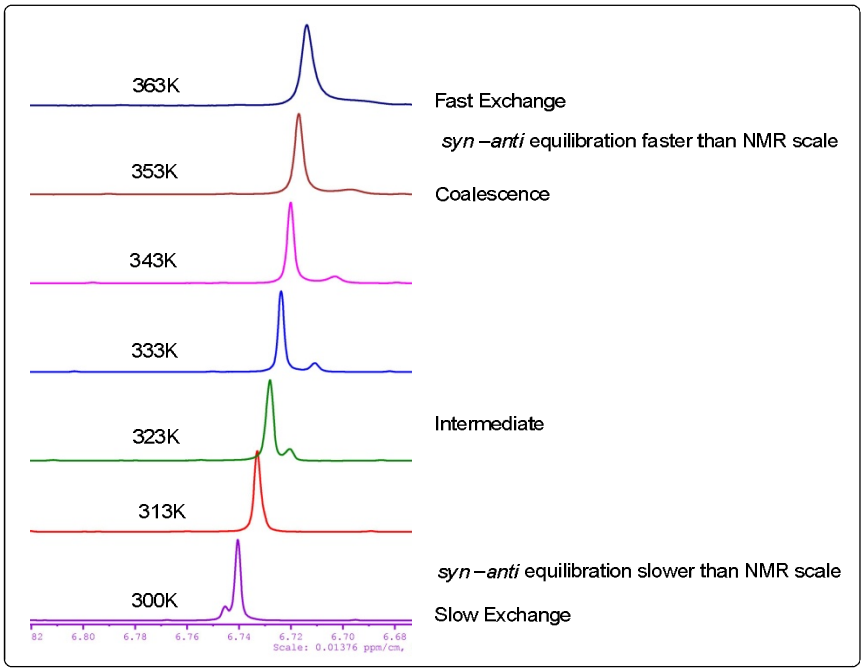


Figure 14

In case of compound **31**, the two sets of peaks were well resolved at 300K and on increasing temperature the two peaks coincide to give a broad singlet. Coalescence for the methylene (-CH_2) and methyl (-CH_3) systems takes place at 353 and 343 K, respectively, The ^{1}H-NMR spectrum then gradually evolves to what is finally observed at 358 K,where only one set of well-resolved signals can be identified (Figure 15). By coalescence temperature (*Tc*) method, we calculated the free-activation energy ($\Delta G^{\ddagger}$ 80.31 kJ/mol, Table 1).

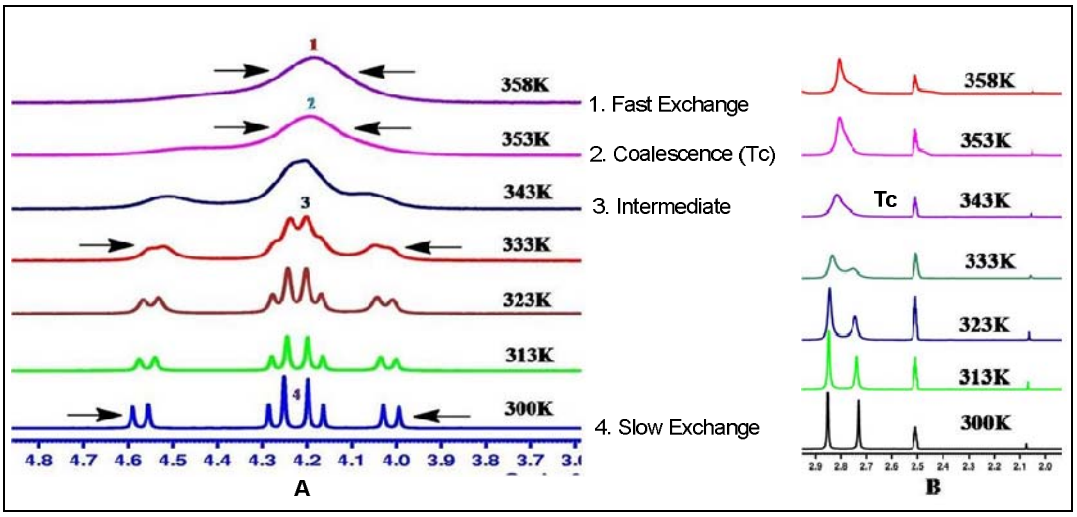


Figure 15: Stacked plot of the VT ^{1}H NMR spectra of terphenyl **31.** A). Ar-**CH_2**-Br region. B). Ar-CH_3 region.

Terphenyl compound **31** indeed exists as a mixture of *syn* and *anti* stereoisomers, which do not interconvert at 230 K. Decreasing the temperature from 300 to 230 K (CD_2Cl_2) did not bring about significant changes in the ^{1}H NMR spectra of **31**, Actually, the fact that no coalescence phenomenon occurs in this temperature range, the signals are shifted to lowfield (Figure 16).

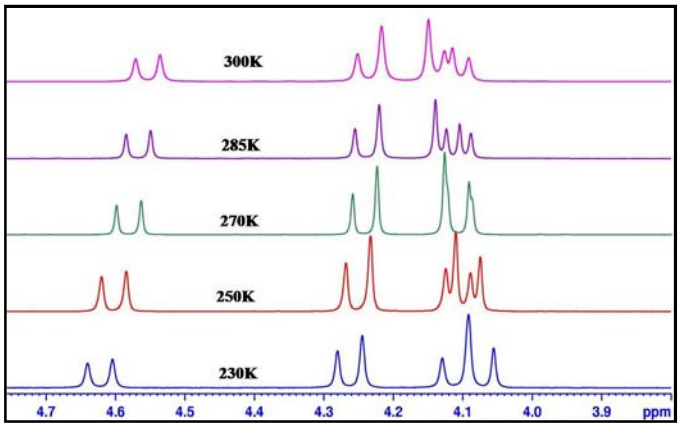


Figure 16: Stacked plot of the low temperature^{1}H NMR spectra of terphenyl **31** in CD_2Cl_2 (Ar-**CH2**-Br region).

Compound **31** was crystallized from acetonitrile to furnish a colorless single crystal, which was analysed by X-ray crystal diffraction. It is expected that the flanking phenyl rings are orthogonal to the central one (such as in Figure 18), owing to atropisomerism. In this situation, there are *syn* and *anti* isomers, as illustrated in Figure 17. Indeed one of these conformations is adopted in the solid state, as seen in the single crystal X-ray crystal structure analysis of terphenyl **31** (Figure 18), in which the *syn* isomer is evident. The angles between the central benzene ring and the mean planes through the *ortho*-substituted phenyl rings are 68.68 and 61.07 respectively.

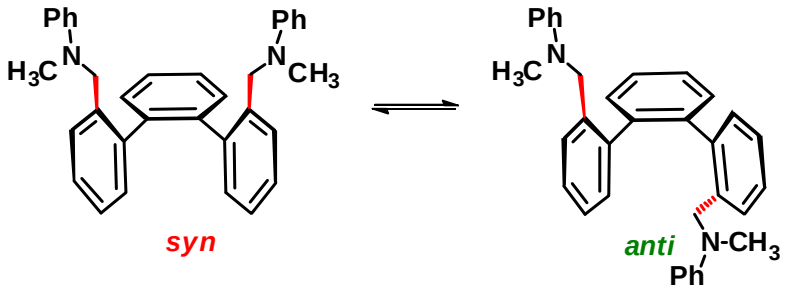


Figure 17: *Syn* and *anti* atropisomers of N,N'-([1,1':2',1''-terphenyl]-2,2''-diylbis(methylene))bis(N-methylaniline) **31**.

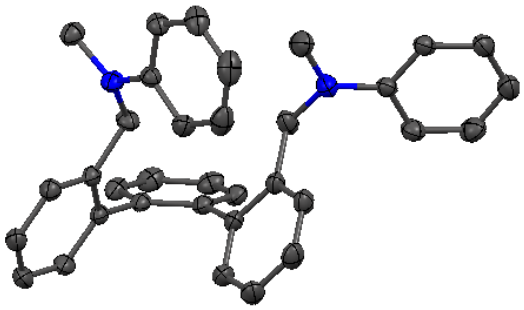


Figure 18: ORTEP view of the X-ray crystal structure of *ortho*-terphenyl **31**. Ellipsoids are drawn at the 40% probability level (CCDC 1424142).

The room-temperature H-NMR spectra of **31**, **33**, **34** and **36** displayed well resolved signals. In VT-NMR analysis, on raising the temperature the *syn* isomer and the *anti* isomer signals broaden and coalesce, eventually yielding a single line. A stacked plots of its variable-temperature (VT) ^{1}H-NMR spectrums are presented in Figure 19. From coalescence temperature (*Tc*) method, the free-activation energy $\Delta G^{\ddagger}$ of all compounds were calculated and summarized in Table-1.

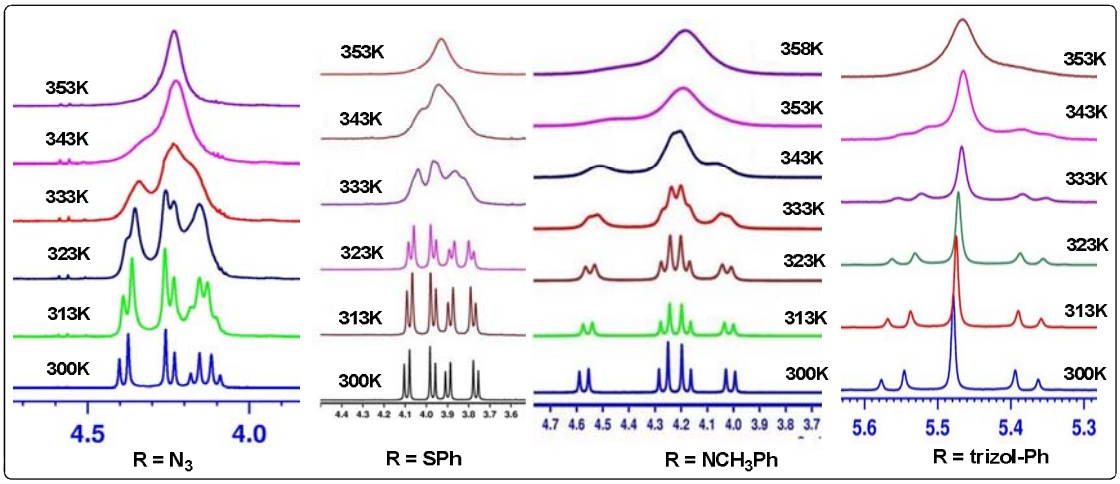


Figure 19: Variable Temperature H-NMR of terphenyl derivatives

Table 1: Observed coalescences and calculated free-activation energies from the VT ^{1}H NMR spectra of terphenyls in DMSO-d_6 at 500 MHz.

Name of compound	Δν (Hz)	Coalescence temperature T_c (K)	Rate constant (sec^{-1})	ΔG (kcal/mol)	kJ/mol
18	6.72	363	14.907	19.43	84.36
31	4.30	353	9.546	19.19	80.31
33	4.03	353	8.769	18.81	80.55
34	4.30	343	9.546	18.22	77.98
36	5.46	343	12.121	18.46	77.27
37	9.73	323	21.60	16.98	71.05
39	4.65	333	9.501	17.62	75.61

In literature the dynamic properties of various *ortho*-terphenyl derivatives (Figure 20) have been reported.[58] Gruza and co-authors[56d] reported a series of terphenyls backbone and have calculated and compared $\Delta G^{\ddagger}$ values for all the compounds, while the maximum value of $\Delta G^{\ddagger}$ was found to be 65 kJ/mol. In contrast, our systems showed higher $\Delta G^{\ddagger}$ values up to 84 kJ/mol. This increasing the $\Delta G^{\ddagger}$ values can be attributed to the higer crowding at *ortho* position due to further derivatization of *ortho* $-CH_3$ group. The $-CH_2$-X group on the *ortho* position further leads to restriction of rotation as is also reflected in the $\Delta G^{\ddagger}$ value.

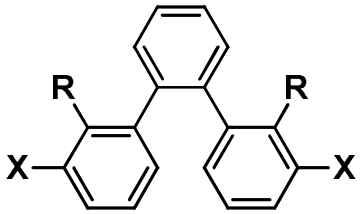


Figure 20: Other *ortho*-terphenyls of the literature (see Table 2 for the references).

Table 2: Calculated free-activation energies for various *ortho*-terphenyls

Compound [a]	R	X	T_c [K] [b]	$\Delta G_c^{\ddagger}$ [kJ/mol]	Ref.
6	CH3	H	282	61.9	20
40	OCH3	H	n.a	n.a	20
41	CH3	Cl	331	73.7	20
42	OH	*t*Bu	300	62.0	56d
43	OCH3	*t*Bu	300	63.1	56d
			330	65.3	
44	H	*i*pr	-	32.2	56b

[a] See Figure 20. [b] Coalescence temperatures used to calculate $\Delta G^{\ddagger}$

As described by Oki[59], the minimum energy barrier requiredfor separation of isomers at room temperature is $\Delta G > 85$ kcal/mol. From the results obtained we could conclude that the barrier to rotation of all the compounds was found to be in the range of 71.05-84.36 kJ/mol. i.e. less than 85 kcal/mole and hence we could not separate *syn* and *anti* isomers at room temperature.

2.3 Conclusion

These molecules display a restricted rotation about the Ar-Ar bond. The barriers of rotation about the Ar-Ar were measured by dynamic ^{1}H-NMR and were found to vary between 71 and 84 kJ/mol, depending on the substitution. In particular, barrier to rotation of all compounds are low ($\Delta G^{\ddagger}$ <85kJ/mol) and could not be isolated as both *syn* and *anti*-isomers at room temperature. The X-ray structure of *N*,*N*'-([1,1':2',1''-terphenyl]-2,2''diylbis(methylene)) bis(*N*-methylaniline) showed *syn* form in solid state.

Calculation of free-activation energy using VT NMR

Variable temperature NMR studies were undertaken in order to calculate free-activation energy, $\Delta G^{\ddagger}$ for all molecules. The general method for calculation of free-activation energies using VT-NMR is described below. As the temperature of the NMR sample increases or decreases there is an increase or decrease in the rate of interconversion which is observed as coalescence /decoalescence of the -CH_2-R AB-type splitting. It is possible to use the temperature of coalescence of these signals to measure the rate of rotation and barrier of rotation about the axis.

The ^{1}H NMR spectrum is obtained at a temperature low enough for the interconverting groups to be at their slow-exchange limit. This is done to obtain the chemical shift difference $\Delta\upsilon$ between the interconverting signals or the coupling constant of the diastereotopic protons, J_{AB}. The sample is gradually heated and spectra are recorded at regular temperature intervals to find the coalescence temperature T_c of the signals.

The rate of exchange, k, at the coalescence temperature T_c can be estimated using the Gutowski-Holm approximation.[61]

$k = \frac{\pi\Delta\upsilon}{\sqrt{2}}$(For uncoupled signals) or

$$k = \pi\sqrt{\frac{(\Delta\upsilon)^2 + 6\,(J_{AB})^2}{2}}$$

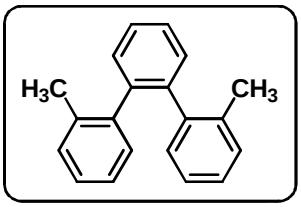
From the approximated value of k and coalescence temperature method17, $\Delta G^{\ddagger}$ can be found to estimate the free energy of activation using the Eyring equation:

$$\Delta G^{\ddagger} = 4.575 \times 10^{-3} \times \mathrm{T_c} \times \left[10.319 + \log_{10}\left(\frac{\mathrm{T_c}}{k}\right)\right]$$

2.4 Experimental Procedures

Reagents were purchased from Sigma-Aldrich Chemicals Limited, SD Fine, Qualigens Limited etc. Thin Layer Chromatography was performed on Merck 60 F_{254} Aluminium coated plates. The spots were visualized under UV light or with iodine vapour. All the compounds were purified by column chromatography using silica gel (60-120 mesh). All the products were characterized by H-NMR, IR, Mass spectroscopy and by comparison of m.p. with the reported values. ^{1}H NMR spectra were recorded on Bruker Avance 400 Spectrometer and were run in $CDCl_3$. Mass spectra were recorded on Thermo-Fischer DSQ II GCMS instrument. IR spectra were recorded on a Perkin-Elmer FTIR RXI spectrometer as KBr pallets. Melting points were recorded in Thiele's tube using paraffin oil and are uncorrected.

2,2''-dimethyl-1,1':2',1''-terphenyl (6)



To an oven dried two-necked round-bottom flask equipped with a stir bar was charged 1,2 dibromo benzene **14** (1 g, 4.24 mmol), 2-methyl phenylboronic acid **15** (1.44 g, 10.5 mmol), $Pd(OAc)_2$ (19 mg,0.08 mmol), dppp (76.9 mg, 0.09mmol) and K_2CO_3 (2.34 g, 16.9 mmol), TBAB (0.55, 1.69 mmol) in dioxane water (1:1, 20 mL) was stirred at 100 ^oC for 24 h. The resulting mixture was allowed to come to room temperature, quenched with water, and extracted with ethyl acetate. The combined organic layers were dried over Na_2SO_4 and concentratedin vacuo. Purification by chromatography on silica gel (Petroleum ether) afforded 0.887 g (81%) of white solid with low melt containing *syn* and *anti* isomers of **6**, and mono product 0.089 g (8%) **16**.

Colorless oil (Lit.[20] 39 - 41^oC).

^{1}H-NMR ($CDCl_3$, 400 MHz): δ 7.40 - 7.32 (m, 4H), 7.07 - 6.87(m, 8H), 2.12 (s, 3H), 2.05 (s, 3H).

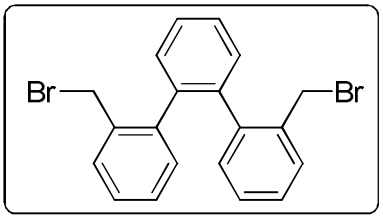
MS (EI) *m/z*, (%): 258 (54), 257 (100), 244 (10), 242 (99), 241 (16), 239 (19), 229 (25), 227 (72), 226 (16), 214 (29), 201 (18), 164 (24).

2-Bromo-2'-methyl-biphenyl (16)[60]

Yield**:** 8% (0.089 g), Colorless oil.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ 7.64 - 7.59 (m, 1H), 7.32 - 7.12 (m, 6H), 7.08 (d, *J* = 7.6 Hz, 1H), 2.09 (s, 3H).

2,2''-bis(bromomethyl)-1,1':2',1''-terphenyl (17)



To a solution of 2,2''-dimethyl-1,1':2',1''-terphenyl **6** (0.500 g, 1.93 mmol) in 50 mL CCl_4, N-bromosuccinimide (1.03 g, 5.81 mmol) and benzoyl peroxide (23 mg, 0.009 mmol) were added. The solution was refluxed under light for 4 h. The resulting mixture was cooled to RT, and the succinimide was removed by filtration; the filtrate was washed with 5% $NaSO_3$ (aq) (3 × 100 mL) and dried with anhydrous Na_2SO_4. The solvent was evaporated. Purification by chromatography on silica gel (Petroleum ether) afforded 0.495 g (61%) of white solid containing *syn*- and *anti*-isomers of **17** in a ratio of 63:37.

M.p. 146-148^{o}C.

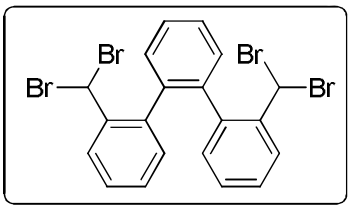
^{1}H-NMR ($CDCl_3$, 400 MHz): δ 7.56- 7.52 (m, 3.22H), 7.45 - 7.39(m, 1.67H), 7.24 – 7.17 (m, 1.63H), 7.15 – 7.11 (m, .62H), 7.07 – 7.03 (m, 1.64H), 6.91 – 6.89 (m, 0.99H), 4.52 – 4.49 (d, *J* = 10Hz, 1.00H), 4.39 – 4.36 (d, *J* = 10.4Hz, 1.01H), 4.29 – 4.23 (AB-type splitting *J* = 10Hz, 1.21H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ 140.35, 139.87, 138..89, 138.83, 135.39, 135.14, 131.73, 130.82, 130.70, 130.51, 130.49, 127.87, 127.82, 127.75, 127.65, 127.54, 32.03, 31.70.

IR (KBr) υ 3046, 3015, 2893, 1684, 1653, 1561, 1465, 1217, 1159, 1003, 867, 779, 759 cm^{-1}.

MS (EI) *m/z*, (%): 417 (9), 415 (20), 337 (23), 336 (21), 334 (42), 256 (20), 255 (47), 254 (100), 253 (29), 252 (46), 240 (27), 239 (47), 125 (15), 119 (25), 104 (23), 90 (23).

2,2''-bis(dibromomethyl)-1,1':2',1''-terphenyl (18)



Compound **18** was prepared by same procedure as that of **17**. In this reaction 4 equivalents or excess of NBS was used.

M.p.: 150-152^{o}C.

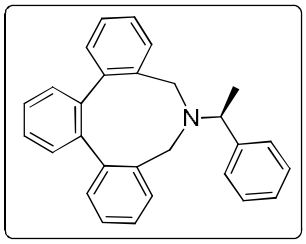
^{1}H-NMR ($CDCl_3$, 400 MHz): δ 7.99-7.97 (dd, *J* = 8 & 0.8 Hz, 1H), 7.59-7.56 (m, 1H), 7.50-7.47 (m, 1H), 7.33-7.29 (m, 1H), 7.04-7.00 (m, 1H), 6.76-6.73 (dd, *J* = 8 & 0.8 Hz, 1H), 6.77 (s, 1H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ 139.81, 138.28, 135.51, 130.29, 130.09, 129.85, 129.05, 128.65, 128.32, 39.51.

MS (EI): *m/z*, (%) 574 (2), 495 (3), 494 (2), 492 (5), 414 (11), 412 (28), 410 (8), 333 (26), 332 (20), 330 (40), 253 (30), 251 (100), 249 (14), 125 (14).

IR (KBr): υ 3066, 3019, 2891, 1560, 1481, 1463, 1430, 1231, 1177, 1158, 1007, 830, 767, 747, 641cm^{-1}.

(*S*)-6-(1-phenylethyl)-6,7-dihydro-5H-tribenzo[c,e,g]azonine (22)



To an oven dried one-necked round-bottom flask equipped with a stir bar was 2,2''-bis(dibromomethyl)-1,1':2',1''-terphenyl **17** (0.200 g, 4.81 mmol), (*S*)-1-phenylethanamine **20** (0.17 g, 1.44 mmol), and K_2CO_3 (0.39, 2.88 mmol) in acetonitrile 10 mL was refluxed at 85 ^oC for 24 h. The resulting mixture was allowed to come to room temperature, quenched with water, and extracted with ethyl acetate. The combined organic layers were dried over Na_2SO_4 and concentrated in vacuo. Purification by chromatography on silica gel (Petroleum ether : ethyl acetate 90:10) afforded 0.155 g (86%) of white solid **22**.

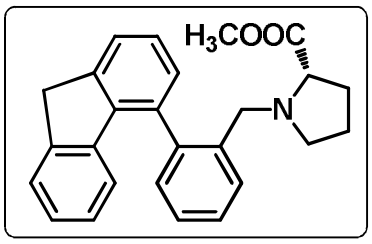
M.p.: 120-122^{o}C.

^{1}H- NMR ($CDCl_3$, 400 MHz): δ 7.54 – 7.41 (m, 4H), 7.39-7.34 (m, 2H), 7.33-7.30 (m, 2H), 7.18-7.15 (m, 1H), 7.09-7.05 (m, 1H), 6.99-6.90 (m, 4H), 6.83-6.76 (m, 3H), 3.99-3.08 (broad signals, 5H), 1.39 (broad signal, 3H).

IR (KBr): υ 3054, 3015, 29922, 2842, 1489, 1471, 1441, 1385, 1319, 1196, 1133, 1096, 1077, 1004, 945, 914, 759, 696 cm^{-1}.

Mass (EI) m/z, (%) 375 (31), 356 (100), 297 (9), 270 (2), 269 (2), 268 (3), 267 (4), 265 (2), 256 (2), 255 (8), 254 (7), 253 (5), 252 (7).

(*S*)-methyl 1-(2-(9H-fluoren-4-yl)benzyl)pyrrolidine-2-carboxylate (25)



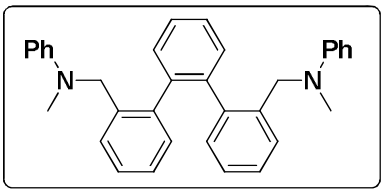
To an oven dried one-necked round-bottom flask equipped with a stir bar was 2,2''-bis(dibromomethyl)-1,1':2',1''-terphenyl **17** (0.150 g, 0.36 mmol), (S)-methyl pyrrolidine-2-carboxylate **23** (1.40 g, 1.05 mmol), and K_2CO_3 (0.29, 2.16 mmol) in acetonitrile 10 mL was refluxed at 85 ^oC for 24 h. The resulting mixture was allowed to come to room temperature, quenched with water, and extracted with ethyl acetate. The combined organic layers were dried over Na_2SO_4 and concentrated in vacuo. Purification by chromatography on silica gel (Petroleum ether : ethyl acetate 90:10) afforded 0.058 g (42%) of white solid **25**.

M.p.: 140-142^{o}C.

^{1}H- NMR ($CDCl_3$, 400 MHz): δ 7.37 – 7.35 (m, 3H), 7.24 (dt, *J* = 7.6 & 1.6 Hz, 1H), 7.20 (dd, *J* = 7.2 & 1.6 Hz, 1H), 7.17 – 7.15 (m, 1H), 7.12 -7.06 (m, 3H), 6.98 (td, *J* = 7.2 & 1.2 Hz, 1H), 6.88 (dd, *J* = 7.6 & 1.2 Hz, 1H), 3.67 (s, 3H), 3.39 (d, J = 13.2, 2H), 3.27 (d, *J* = 13.2 Hz, 1H), 3.07 (dt, *J* = 7.6 & 3.2 Hz, 1H), 2.84 (d, *J* = 14.4 Hz, 1H), 2.73 (q, *J* = 8 Hz, 1H), 2.37 – 2.32 (m, 1H), 2.15 – 2.08 (m, 1H), 1.68 – 1.64 (m, 1H), 1.46 – 1.41 (m, 1H).

MS (EI): *m/z*, (%) 382 (2), 324 (75), 323 (100), 255 (13).

N,N'-([1,1':2',1''-terphenyl]-2,2''-diylbis(methylene))bis(N-methylaniline) (31)



To an oven dried one-necked round-bottom flask equipped with a stir bar was 2,2''-bis(dibromomethyl)-1,1':2',1''-terphenyl **17** (0.250 g, 0.60 mmol), methyl aniline **28** (0.19 g, 1.80 mmol), and K_2CO_3 (0.49, 3.61 mmol) in acetonitrile 10 mL was refluxed at 85 ^oC for 24 h. The resulting mixture was allowed to come to room temperature, quenched with water, and extracted with ethyl acetate. The combined organic layers were dried over Na_2SO_4 and concentrated in vacuo. Purification by chromatography on silica gel (Petroleum ether : ethyl acetate 95:5)

afforded 0.189 g (67%) of white solid containing *syn*- and *anti*-isomers of **31** in a ratio of 64:36.

M.p.: 132-134^{o}C.

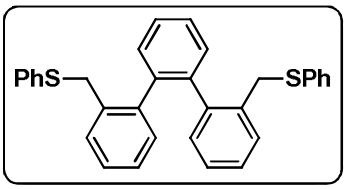
^{1}H- NMR ($CDCl_3$, 400 MHz): δ 7.50 – 7.47 (m, 4.47H), 7.39 – 7.36 (m, 2.16H), 7.28 – 7.25 (m, 4.01H including $CDCl_3$), 7.23 – 7.20 (m, 5.28H), 7.18 – 7.07 (m, 11.96H), 6.69 - 6.43 (m, 3.23H), 6.46 - 6.39 (m, 6.32H), 4.55 (d, *J* = 17.6 Hz, 1H), 4.23 (d, *J* = 17.2Hz, 1.48H), 4.14 - 4.07 (two doublet, *J* = 17.2 & 18 Hz, 2.43H), 2.84 (s, 3.91H), 2.76 (s, 2.44H).

MS (EI): *m/z*, (%) 468 (7), 441 (28), 360 (100), 256 (12), 254 (92).

HRMS (ESI $^{+}$): caluculated mass [M+1] $C_{34}H_{32}N_2$ = 469.2644 founded = 469.2638.

IR (KBr): υ 3055, 2882, 2805, 1598, 1507, 1443, 1375, 1348, 1252, 1212, 1118, 1031, 1000, 953, 867, 747, 692 cm^{-1}.

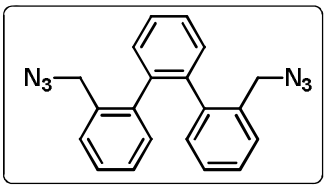
2,2''-bis((phenylthio)methyl)-1,1':2',1''-terphenyl (33)



A solution of thiophenol (0.07 g, 0.61 mmol), KOH (0.15 g, 2.64 mmol) in MeOH (10 mL) was stirred for 10 min. at room temperature, then slowly added 2,2''-bis(dibromomethyl)-1,1':2',1''-terphenyl **17** (0.110 g, 0.28 mmol)and mixture was stirred for 24 h. The crude product was quenched with water. The aqueous layer was extracted with ethyl acetate (3 × 250 mL) and then dried with anhydrous sodium sulfate. The organic solvent was evaporated under reduced pressure to give a pale yellow liquid as crude product, which was purified by column chromatography on silica gel using petroleum ether as eluent to give **33** (0.094 g, 78%) as a colorless oil, contain *syn*- and *anti*-isomers of **33** in a ratio of 56:44.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ 7.46 – 7.41 (m, 3.25H), 7.36 -7.31 (m, 3.51H), 7.24 - 7.15 (m, 9.95H), 7.14 - 7.08 (m, 5.12H), 7.03-6.99 (m, 2.24H), 3.98 – 3.91 (AB splitting *J* = 12.8 Hz, 2.45H), 3.89 – 3. (AB splitting *J* = 12.4 Hz, 1.96H).

2,2''-bis(azidomethyl)-1,1':2',1''-terphenyl (34)



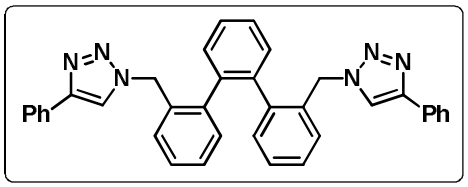
A solution of 2,2''-bis(dibromomethyl)-1,1':2',1''-terphenyl **17** (0.250 g, 0.60 mmol), sodium azide (0.18 g, 0.18 mol) in acetonitrile (30 mL) was refluxed for 24 h. The mixture was cooled to room temperature and solvent was removed at high vacuum, the crude product was quenched with water. The aqueous layer was extracted with ethyl acetate (3 × 250 mL) and then dried with anhydrous sodium sulfate. The organic solvent was evaporated under reduced pressure to give a pale yellow liquid as crude product, which was purified by column chromatography on silica gel using petroleum ether as eluent to give diazide **34** (0.180 g, 88%) as a colorless oil, contain *syn*- and *anti*-isomers of **34** in a ratio of 60:40.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ 7.51 – 7.48 (m, 2.48H), 7.40 -7.30 (m, 5.07H), 7.26 -7.12 (m, 5.90H), 6.98 - 6.96 (m, 1.39H), 4.20 – 4.19 (AB splitting *J* = 13.6 Hz, 3.02H), 4.13 – 4.03 (AB splitting *J* = 13.6 Hz, 2.00H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ 140.49, 140.03, 139.06, 138.94, 133.31, 132.93, 131.00, 130.71, 130.37, 129.04, 128.85, 127.79, 127.75, 127.41, 52.60, 52.24.

MS (EI) *m/z*, (%): 310 [M-N_2+2] (14), 282 (91), 280 (21), 270 (52), 268 (54), 265 (67), 254 (35), 253 (36), 251 (30).

2,2''-bis((4-phenyl-1H-1,2,3-triazol-1-yl)methyl)-1,1':2',1''-terphenyl (36)



A solution of 2,2''-bis(azidomethyl)-1,1':2',1''-terphenyl **34** (0.100 g, 0.29 mmol), CuI (5.6 mg, 0.03 mmol) and phenyl acetalene (0.07 g, 0.74 mmol) in acetonitrile (5 mL) were added at 0 ^{o}C under N_2 atmosphere, and stirred for 24 h. The mixture was monitor by tlc and solvent was removed at high vacuum, the crude product was quenched with water. The aqueous layer was extracted with ethyl acetate (3 × 250 mL) and then dried with anhydrous sodium sulfate. The organic solvent was evaporated under reduced pressure to give a pale yellow liquid as crude product, which was purified by column chromatography on silica gel using petroleum ether as eluent to give diazide **34** (0.180 g, 88%) as a colorless oil, contain *syn*- and *anti*-isomers of **34** in a ratio of 60:40.

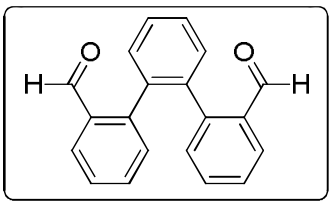
M.p.: 234-238°C.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ 7.77 – 7.74 (m, 4.40H), 7.57 – 7.55 (m, 1.64H), 7.52 -7.43 (m, 1.06H), 7.43 – 7.19 (m, 22.88H including $CDCl_3$), 7.12 (s, 1.49H), 7.06 -7.05 (m, 1.57H), 6.98 - 6.68 (m, 1.01H), 5.59 (AB splitting, d, *J* = 15.2 Hz, 1.00H), 5.34 (AB splitting , d, *J* = 15.2 Hz, 1.63H), 5.25 (AB splitting ,two doublet merged *J* = 15.2 Hz, 2.50H).

HRMS (ESI $^+$): caluculated mass $C_{36}H_{28}N_6$ $[M + Na]^+$ 567.2273, found 567.2266 *m/z*.

IR (KBr): υ 2927, 2857, 1730, 1599, 1464, 1436, 1274, 1127, 1074, 1044, 768, 695 cm^{-1}.

[1,1':2',1''-terphenyl]-2,2''-dicarbaldehyde (37)



To an oven dried one-necked round-bottom flask equipped with a stir bar was 2,2''-bis(dibromomethyl)-1,1':2',1''-terphenyl **17** (0.250 g, 0.60 mmol), $NaHCO_3$ (0.15 g, 1.80 mmol), in DMSO 5 mL was heated at 140 °C for 24 h. The resulting mixture was allowed to come to room temperature, quenched with water, and extracted with ethyl acetate. The combined organic layers were dried over Na_2SO_4 and concentrated in vacuo. Purification by chromatography on silica gel (Petroleum ether : ethyl acetate 90:10) afforded 0.115 g (67%) of white solid containing *syn*- and *anti*-isomers of **37** in a ratio of 36:64.

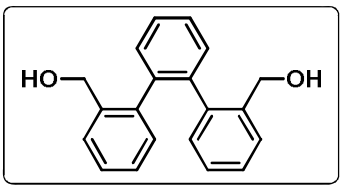
M.p.: 150-152°C.

^{1}H- NMR ($CDCl_3$, 400 MHz): δ 9.85 (s, 1.03H), 9.79 (s, 1.86H), 7.81- 7.75 (m, 2.93H), 7.60 - 7.55 (m, 3.14H), 7.49 – 7.41 (m, 5.98H), 7.38 – 7.33 (m, 3.04H), 7.19 – 7.15 (m, 3H).

MS (EI) *m/z*, (%): 288 (1), 287 (8), 286 (54), 285 (41), 268 (34), 267 (15), 267 (23), 257 (24), 256 (20), 242 (31), 241 (100), 240 (84), 239 (58), 229 (50), 228 (50), 227 (52), 226 (56), 225 (33), 202 (20), 152 (14).

IR (KBr): υ 3371, 3057, 2923, 2833, 2748, 1692, 1651, 1597, 1444, 1394, 1261, 1194, 1124, 1103, 1005, 959, 827, 778, 763, 644, 602.

[1,1':2',1''-terphenyl]-2,2''-diyldimethanol (**39**)

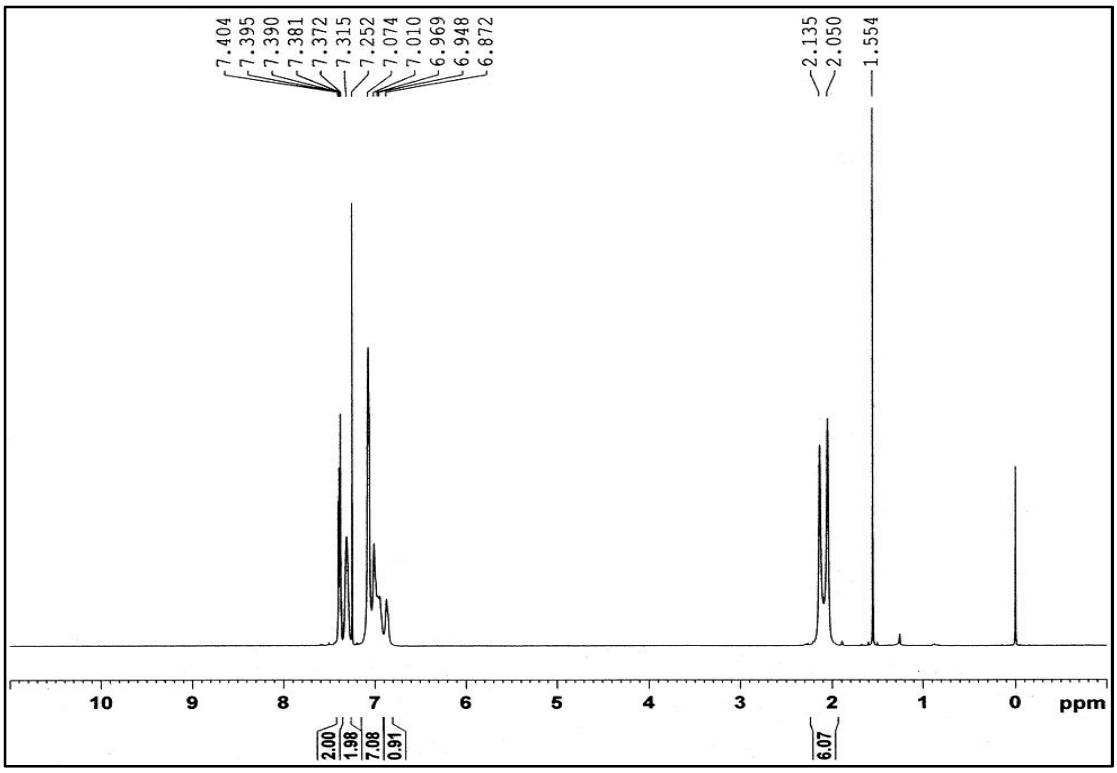


To an oven dried one-necked round-bottom flask equipped with a stir bar was [1,1':2',1''-terphenyl]-2,2''-dicarbaldehyde **37** (0.200 g, 0.69 mmol), $NaBH_3$ (0.08 g, 2.10 mmol), in MeOH 5 mL was stirred at room temperature for 24 h. The resulting mixture was quenched with water, and extracted with ethyl acetate. The combined organic layers were dried over Na_2SO_4 and concentrated in vacuo. Purification by chromatography on silica gel (Petroleum ether : ethyl acetate 90:10) afforded 0.157 g (78%) of white solid containing *syn*- and *anti*-isomers of **39**.

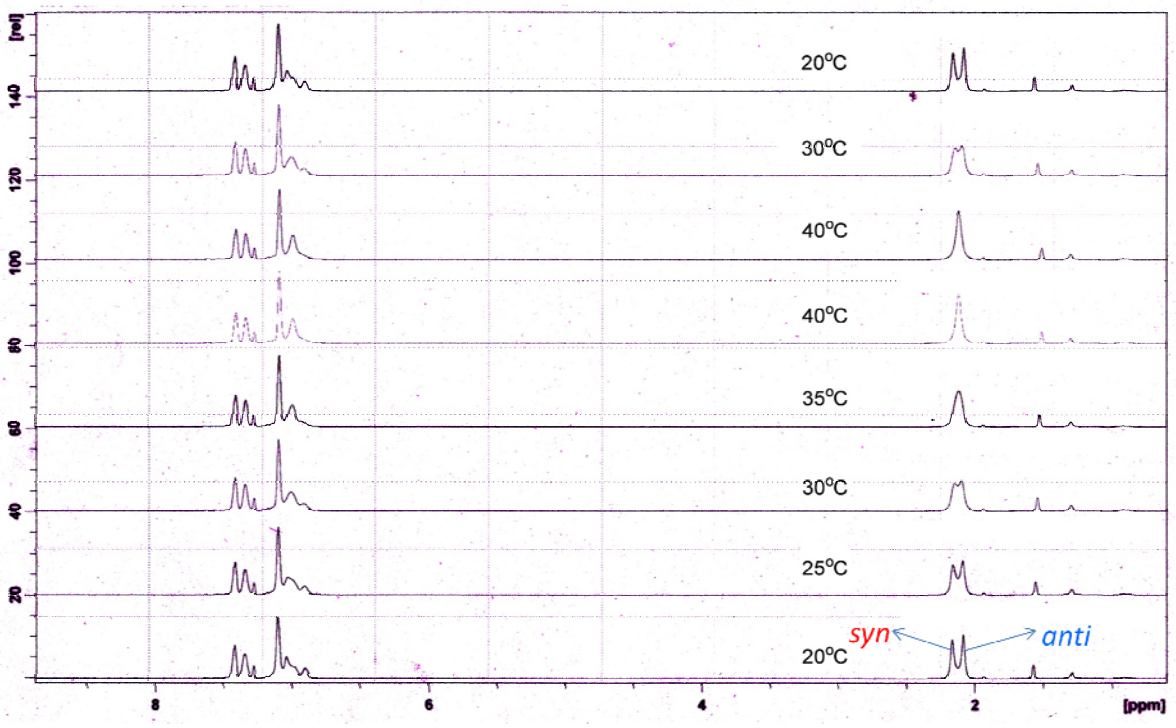
^{1}H- NMR ($CDCl_3$, 400 MHz): 7.54 – 7.51 (m, 0.27H), 7.45 – 7.32 (m, 8.66H), 7.26 -7.23 (m, 2.30H), 7.21 -7.13 (m, 2.96H), 7.11 – 7.08 (m, 2.64H), 4.47 – 4.27 (broad AB splitting 3.52H), 4.40 - 4.30 (broad AB splitting, 2.39H).

MS (EI) *m/z*, (%): 273 [M-OH] (16), 272 (100), 271 (80), 256 (54), 254 (13), 253 (30), 252 (22).

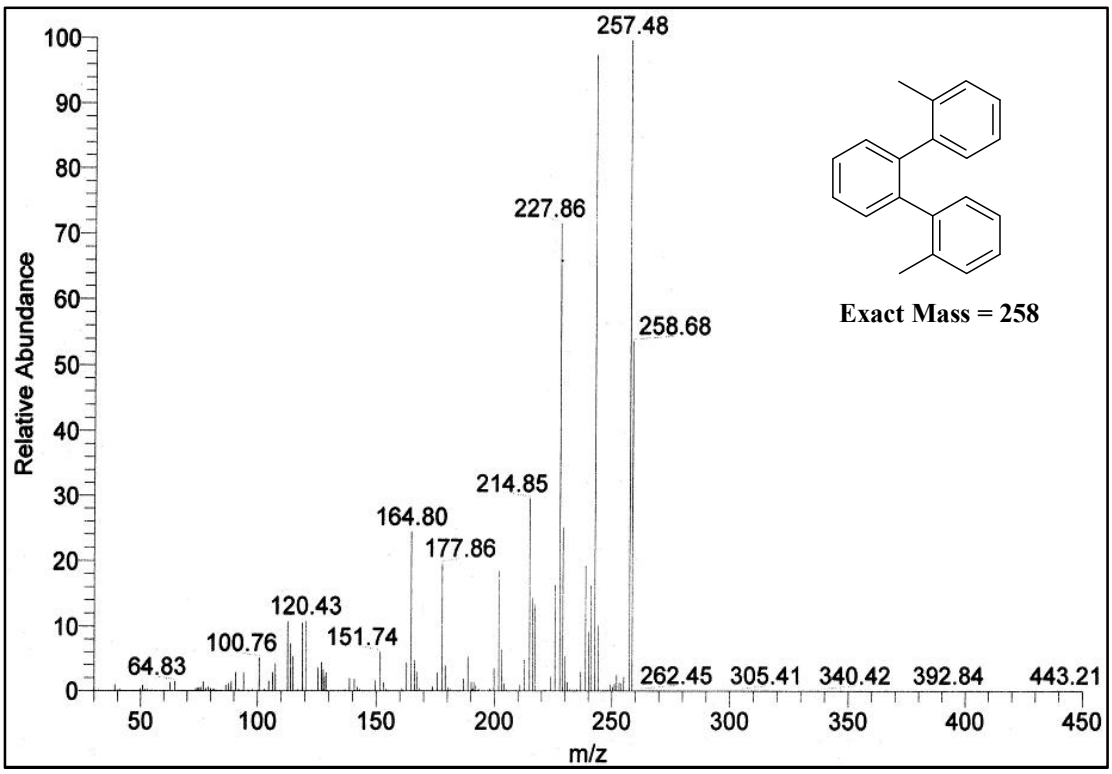
2.5 Spectral reproductions:



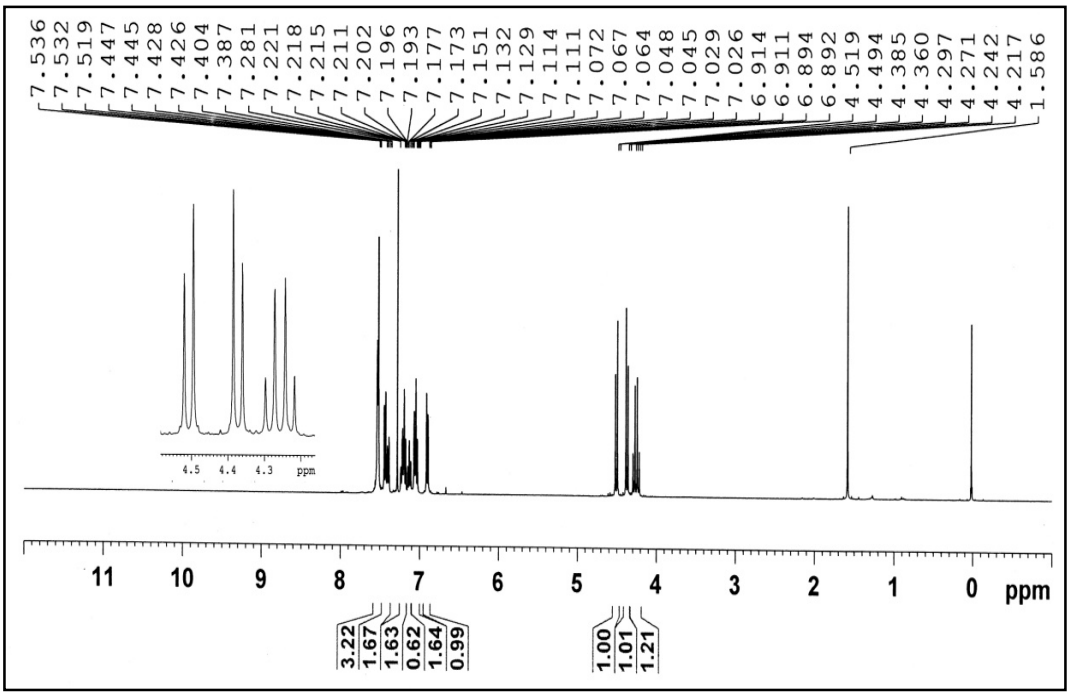
^{1}H-NMR spectrum of 2,2''-dimethyl-1,1':2',1''-terphenyl (6) in $CDCl_3$ on 400 MHz



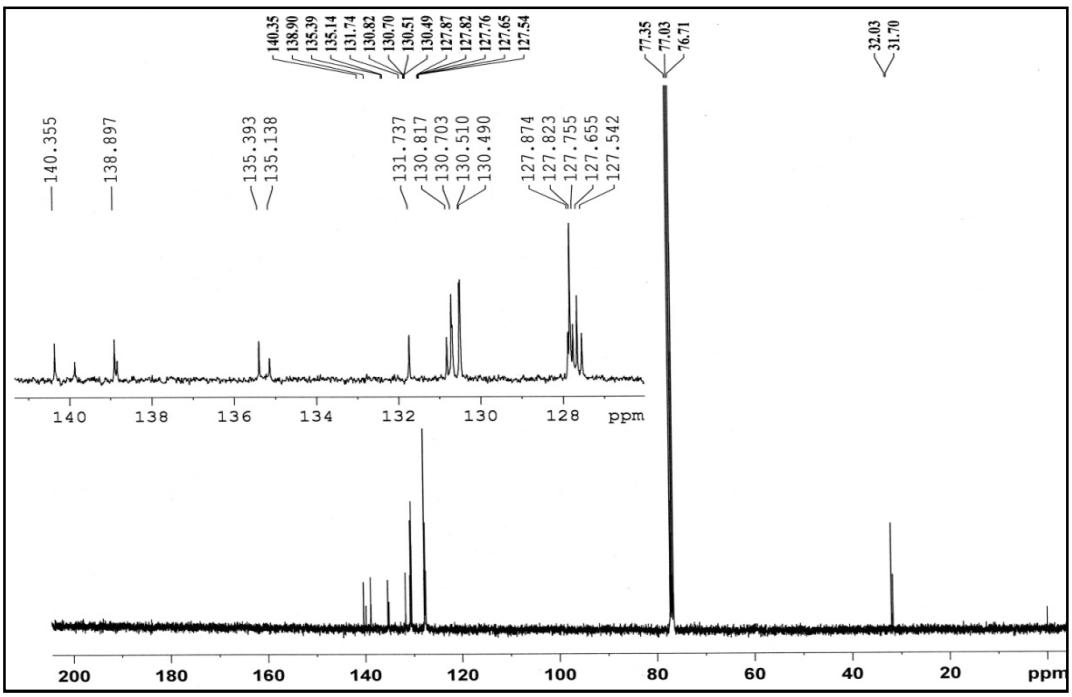
Variable temperature H-NMR of 2,2''-dimethyl-1,1':2',1''-terphenyl (6)



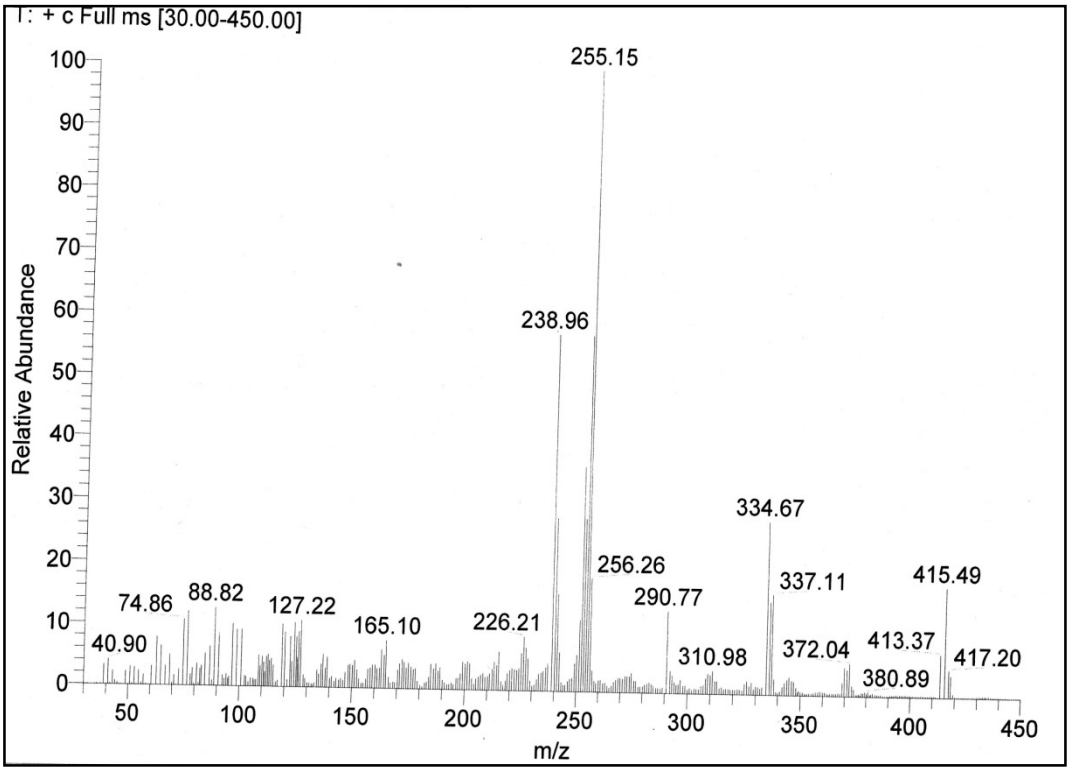
EI-mass spectra of compound 6



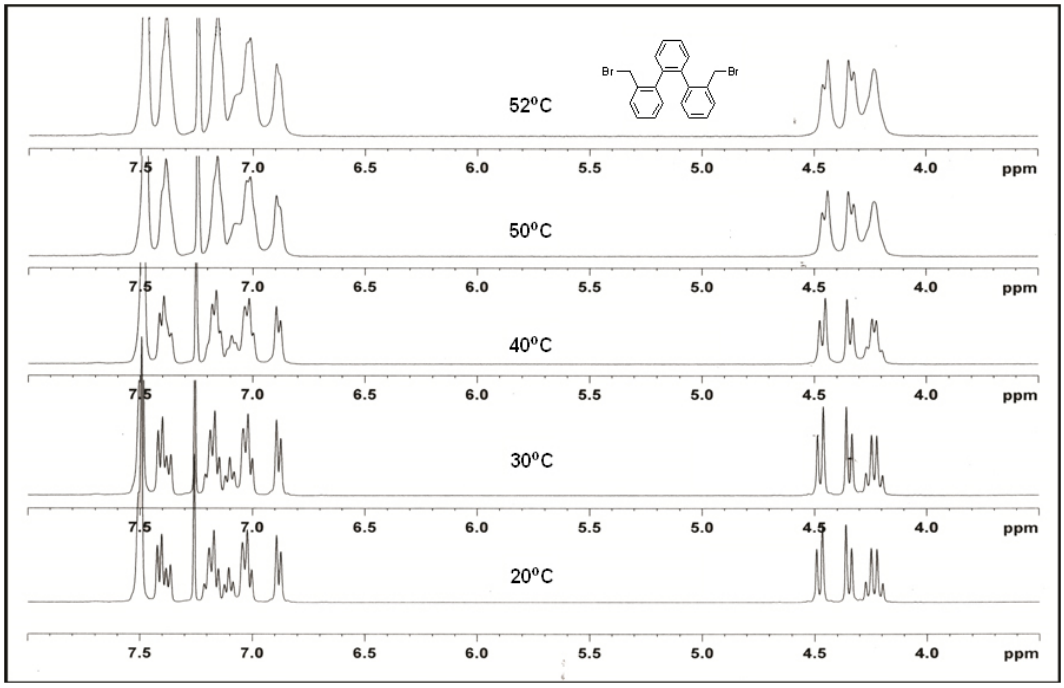
^{1}H-NMR spectrum of 2,2''-bis(bromomethyl)-1,1':2',1''-terphenyl (17) in $CDCl_3$ on 400 MHz



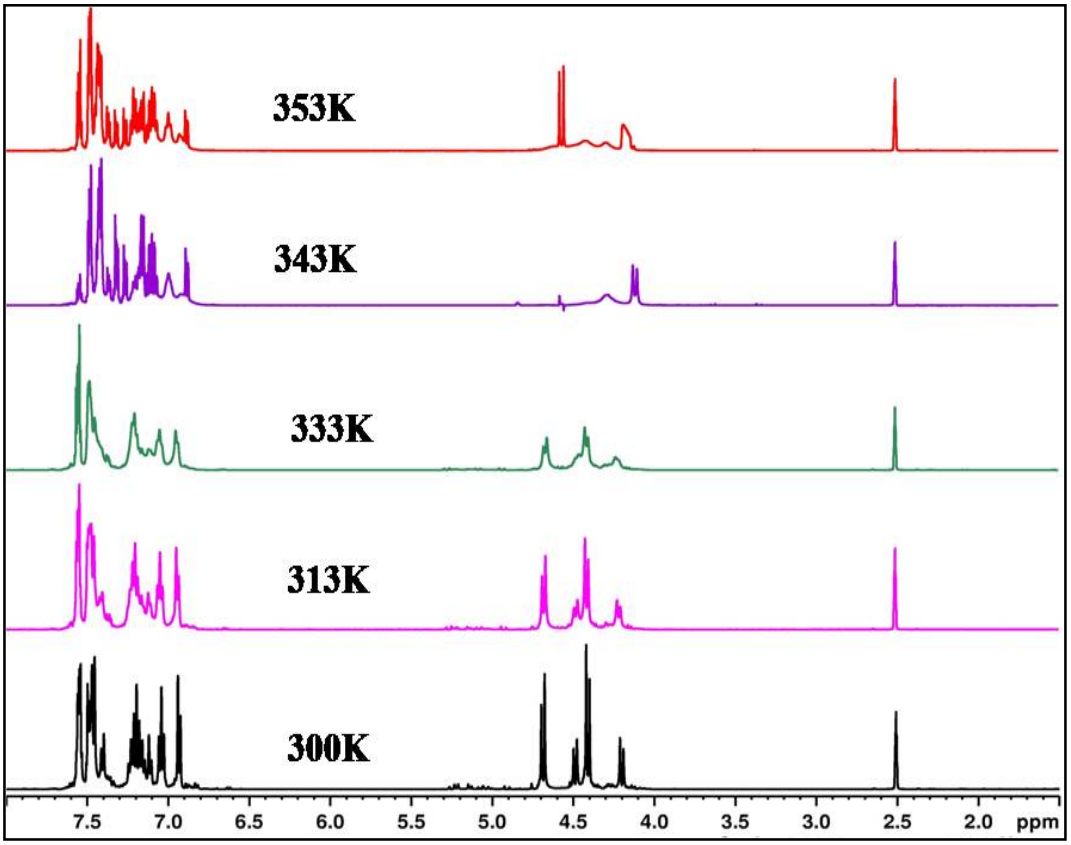
^{13}C-NMR spectrum of 2,2''-bis(bromomethyl)-1,1':2',1''-terphenyl (17) in $CDCl_3$ on 100.6 MHz



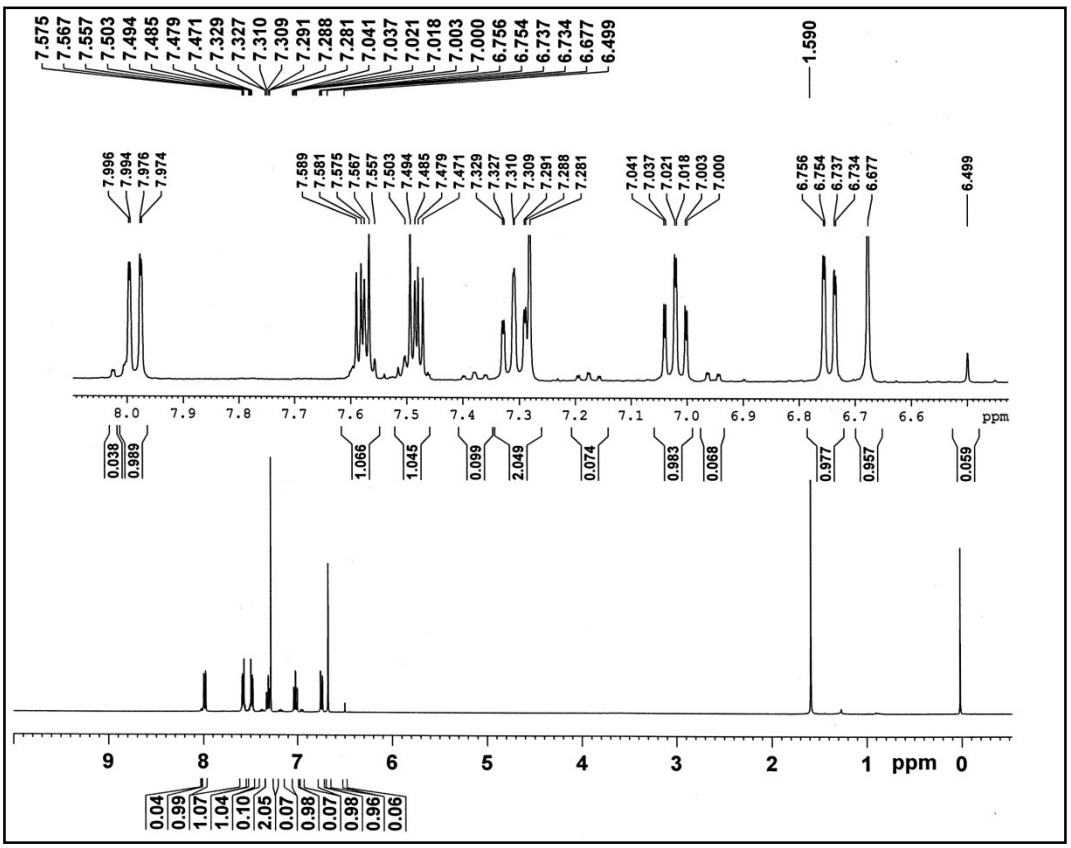
EI mass of 2,2''-bis(bromomethyl)-1,1':2',1''-terphenyl (17)



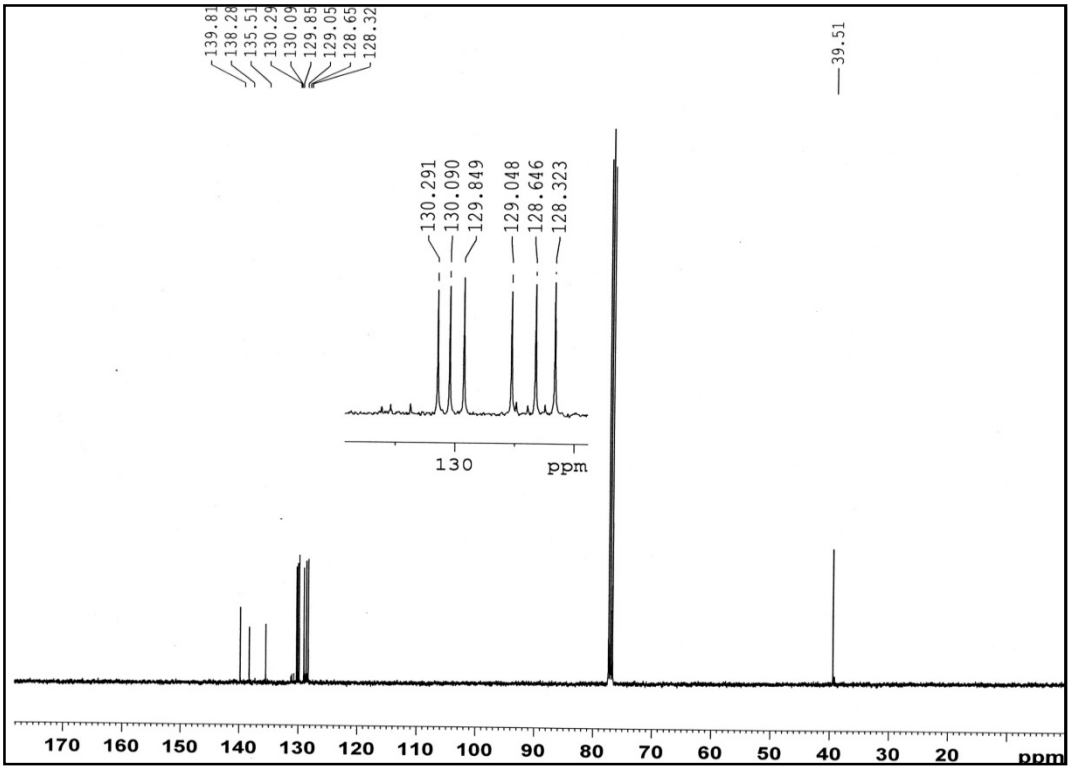
Variable temperature H-NMR of 2,2''-bis(bromomethyl)-1,1':2',1''-terphenyl (17) in $CDCl_3$



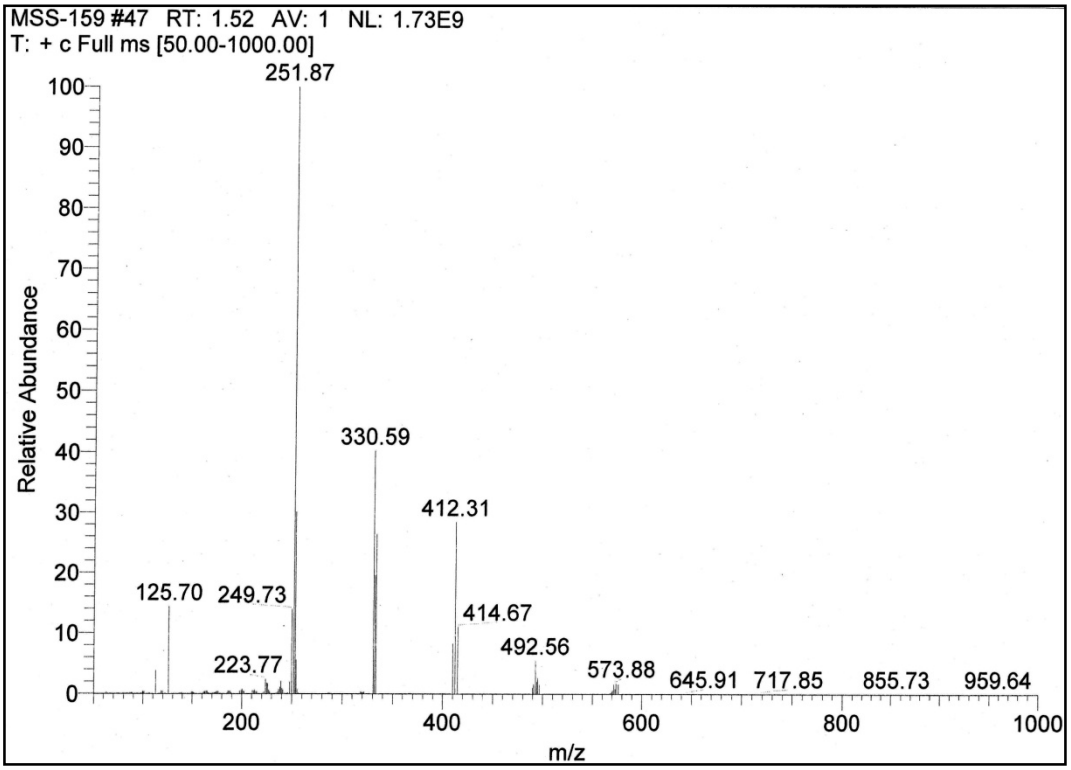
^{1}H NMR spectrum of compound 2,2''-bis(bromomethyl)-1,1':2',1''-terphenyl (17) at different temperature (500MHz, DMSO-d_6,)



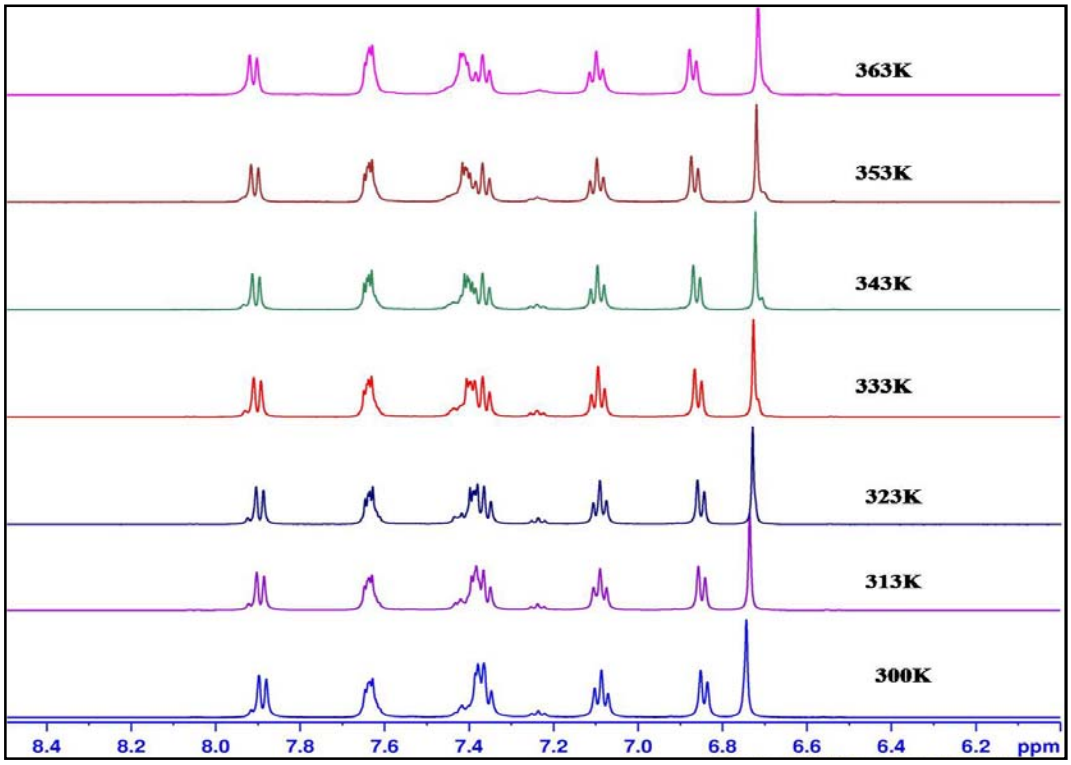
^{1}H-NMR spectrum of 2,2''-bis(dibromomethyl)-1,1':2',1''-terphenyl (18) in $CDCl_3$ on 400 MHz



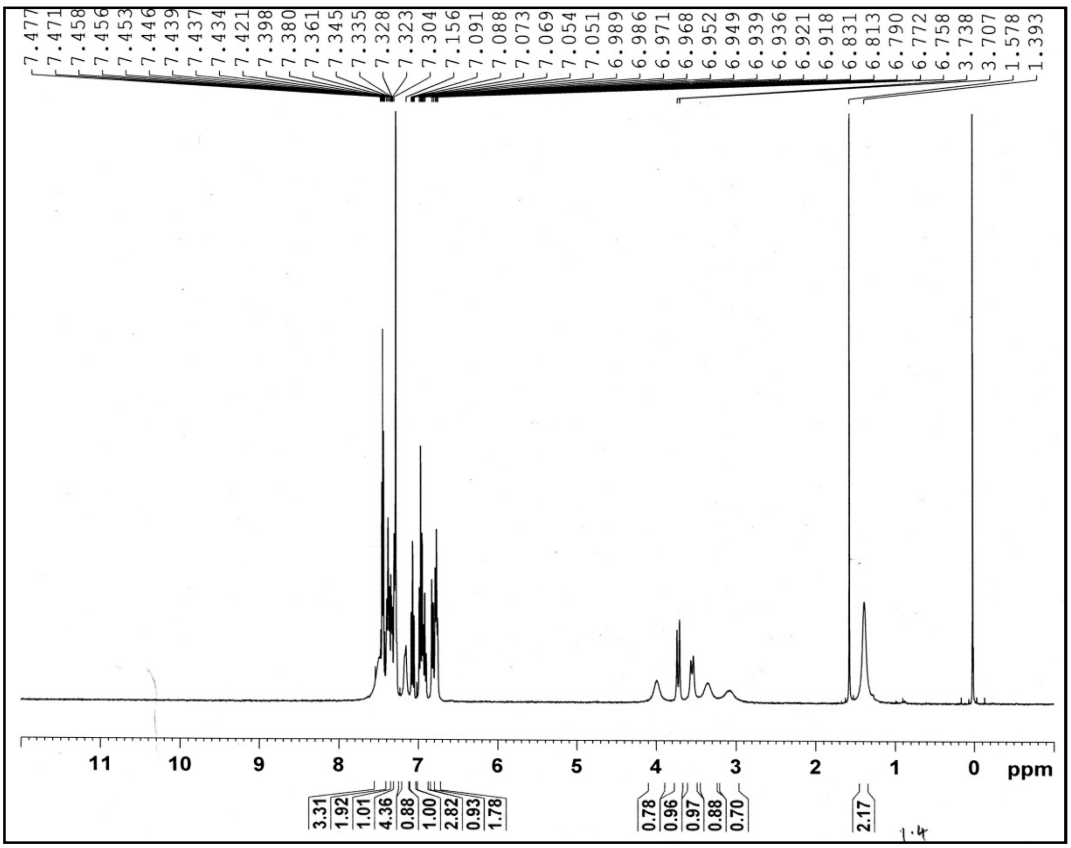
^{13}C-NMR spectrum of 2,2''-bis(dibromomethyl)-1,1':2',1''-terphenyl (18) in $CDCl_3$ on 100.6 MHz



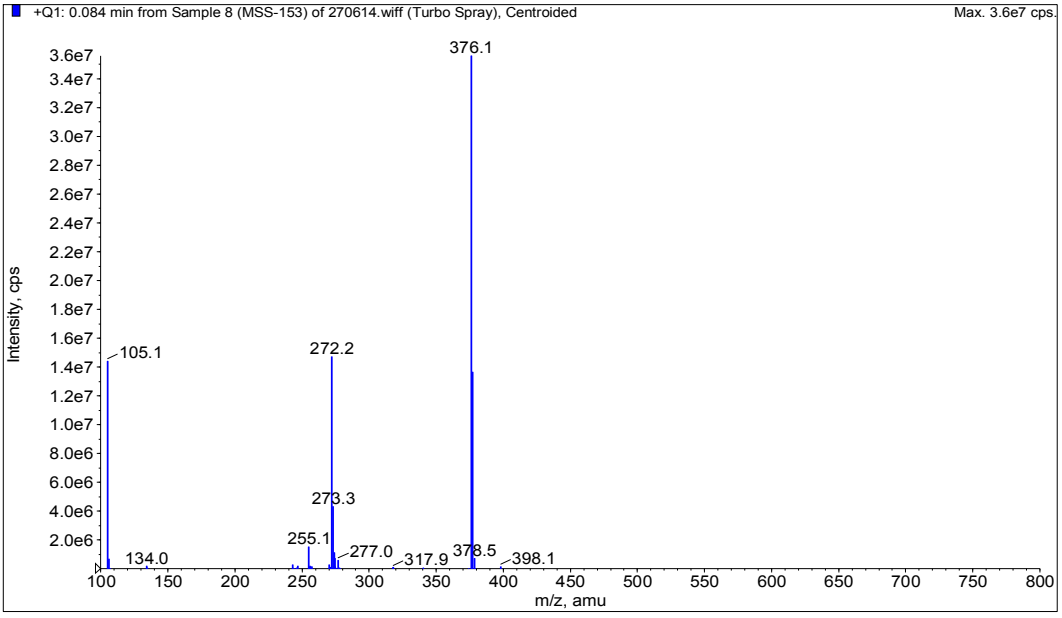
EI mass of 2,2''-bis(dibromomethyl)-1,1':2',1''-terphenyl (18)



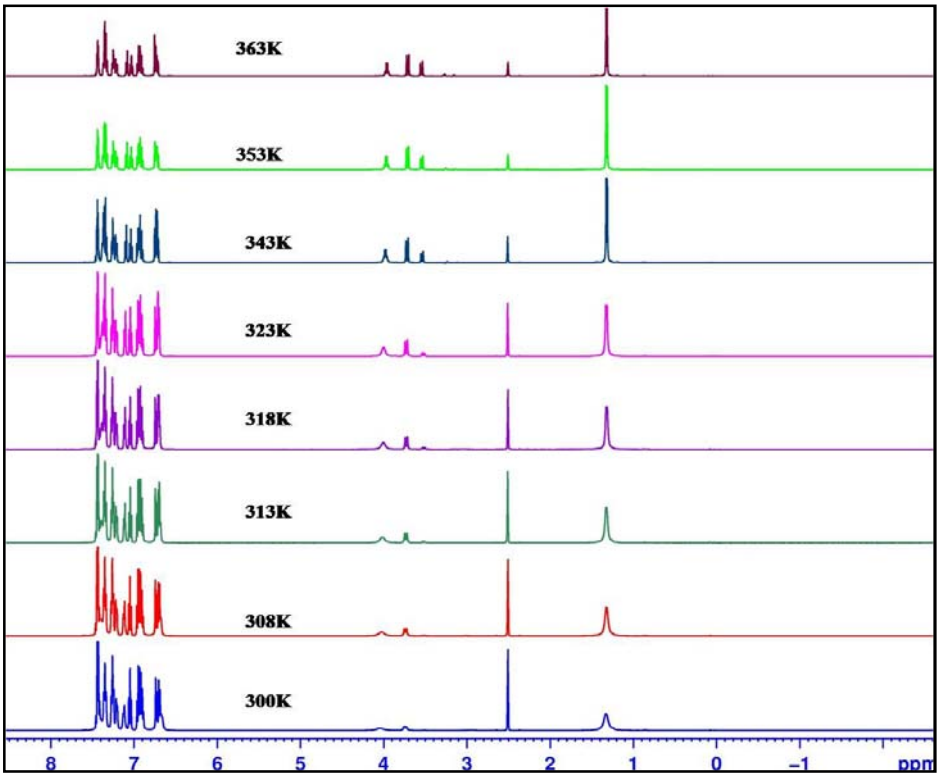
Expansion ^{1}H-NMR spectrum of compound 2,2''-bis(dibromomethyl)-1,1':2',1''-terphenyl (18), Aromatic proton region at different temperature (500MHz, DMSO-d_6,)



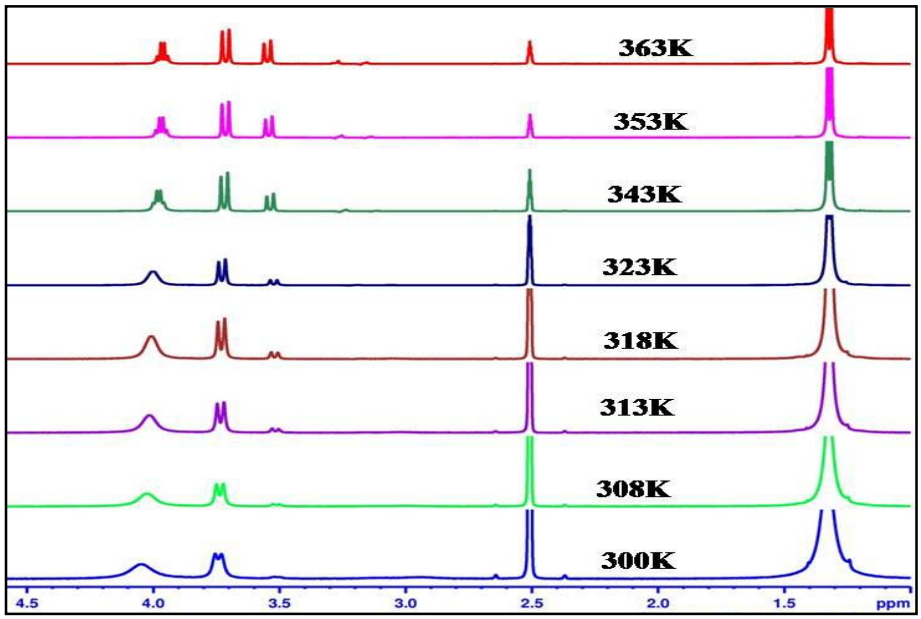
^{1}H-NMR spectrum of (*S*)-6-(1-phenylethyl)-6,7-dihydro-5H-tribenzo[c,e,g]azonine (22) in $CDCl_3$ on 400 MHz



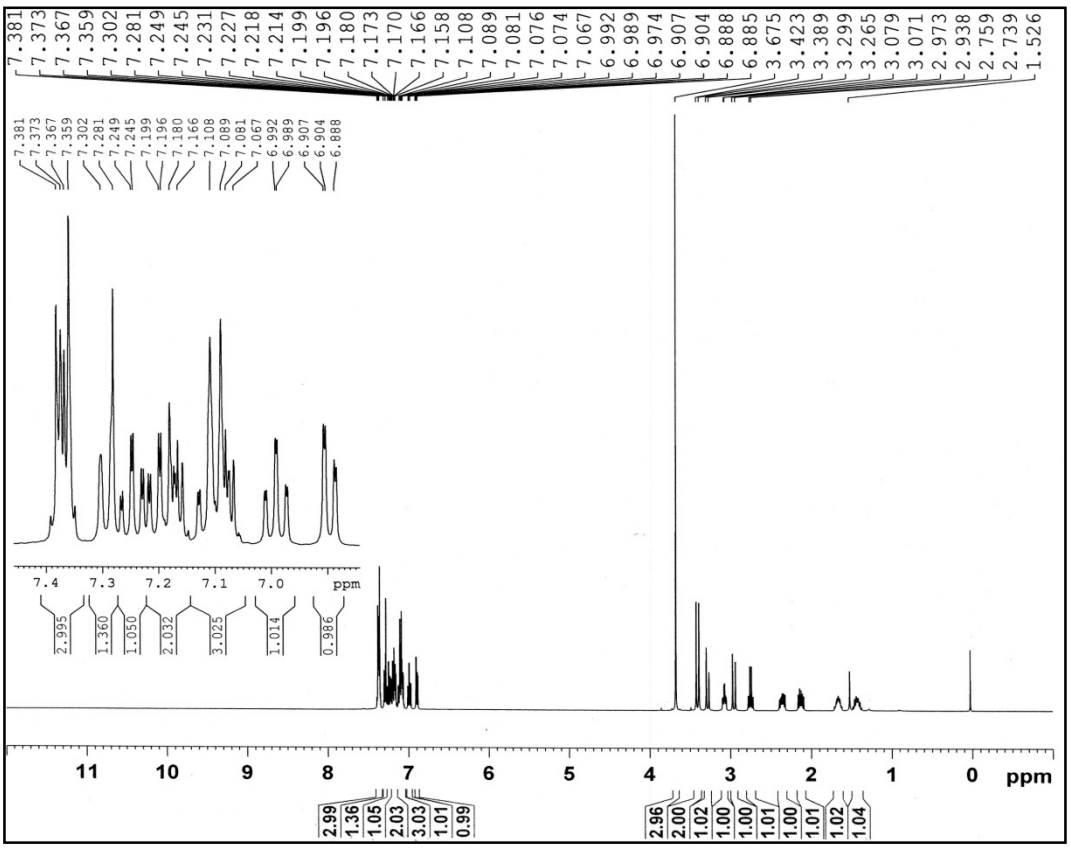
ESI mass of of (*S*)-6-(1-phenylethyl)-6,7-dihydro-5H-tribenzo[c,e,g]azonine (22)



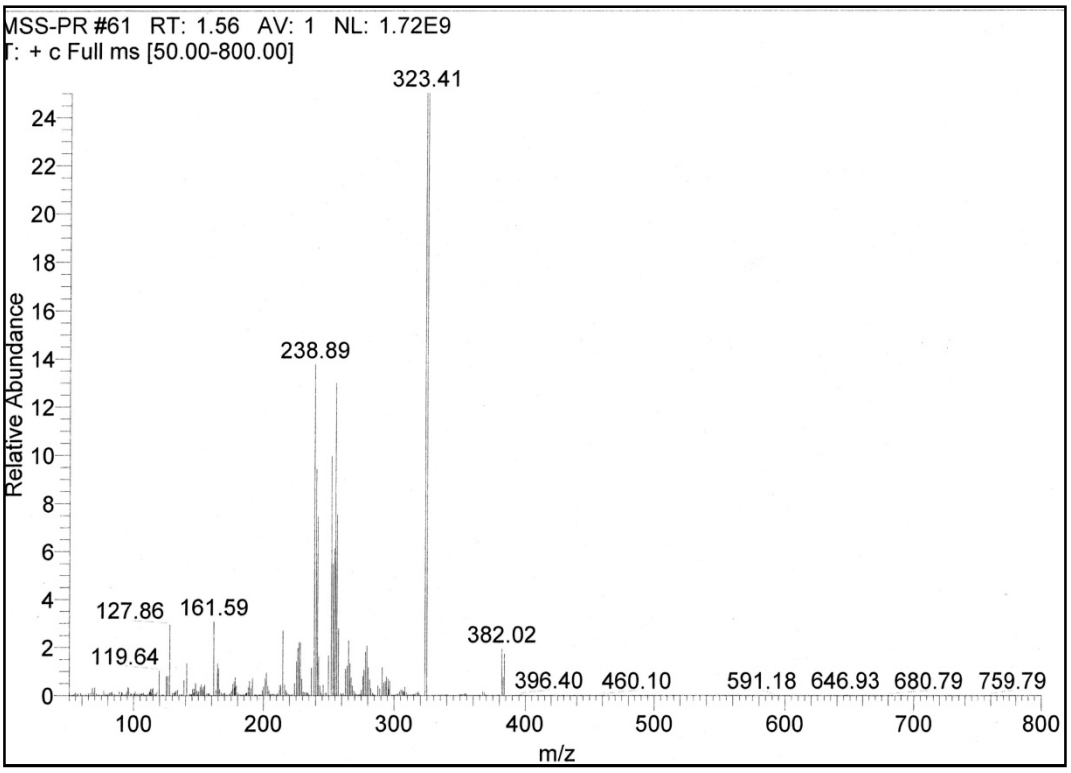
^{1}H NMR spectrum of (S)-6-(1-phenylethyl)-6,7-dihydro-5H-tribenzo[c,e,g]azonine (22) at different temperature (500MHz, DMSO-d_6)



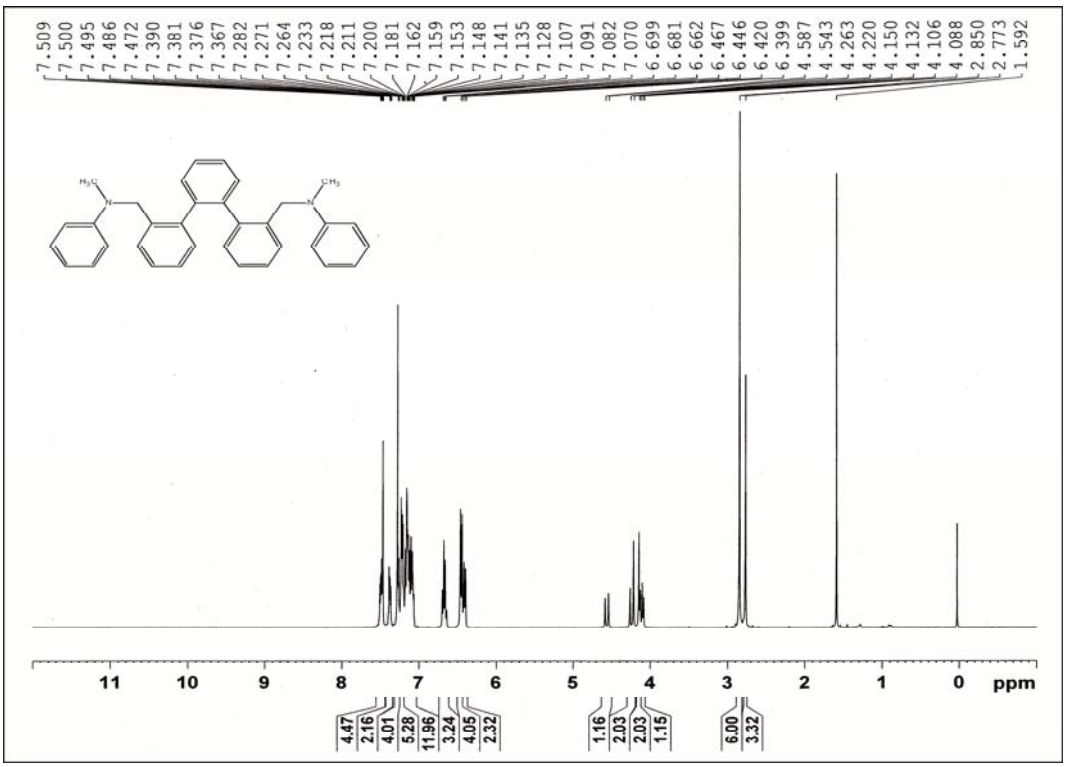
Expansion ^{1}H-NMR spectrum of (*S*)-6-(1-phenylethyl)-6,7-dihydro-5H-tribenzo[c,e,g]azonine (22). Methylene (-CH_2) proton and chiral carbon proton (-CH) region at different temperature (500MHz, DMSO-d_6,)



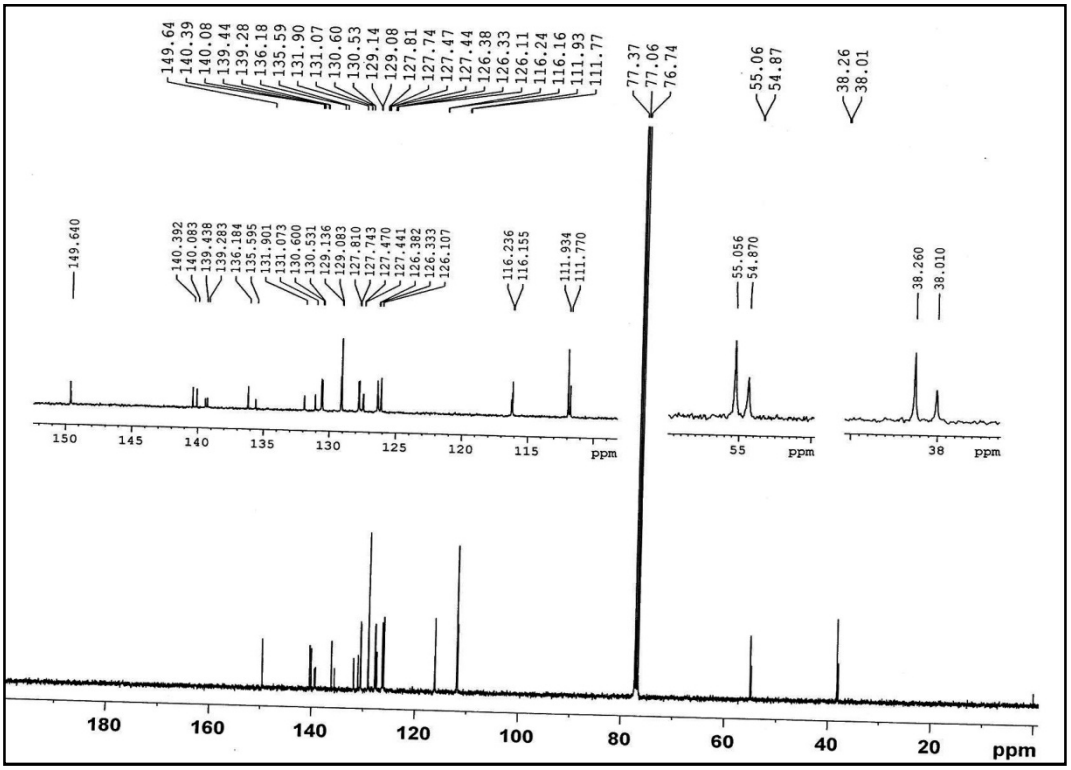
^{1}H-NMR spectrum of (S)-methyl 1-(2-(9H-fluoren-4-yl)benzyl)pyrrolidine-2-carboxylate (25) in $CDCl_3$ on 400 MHz



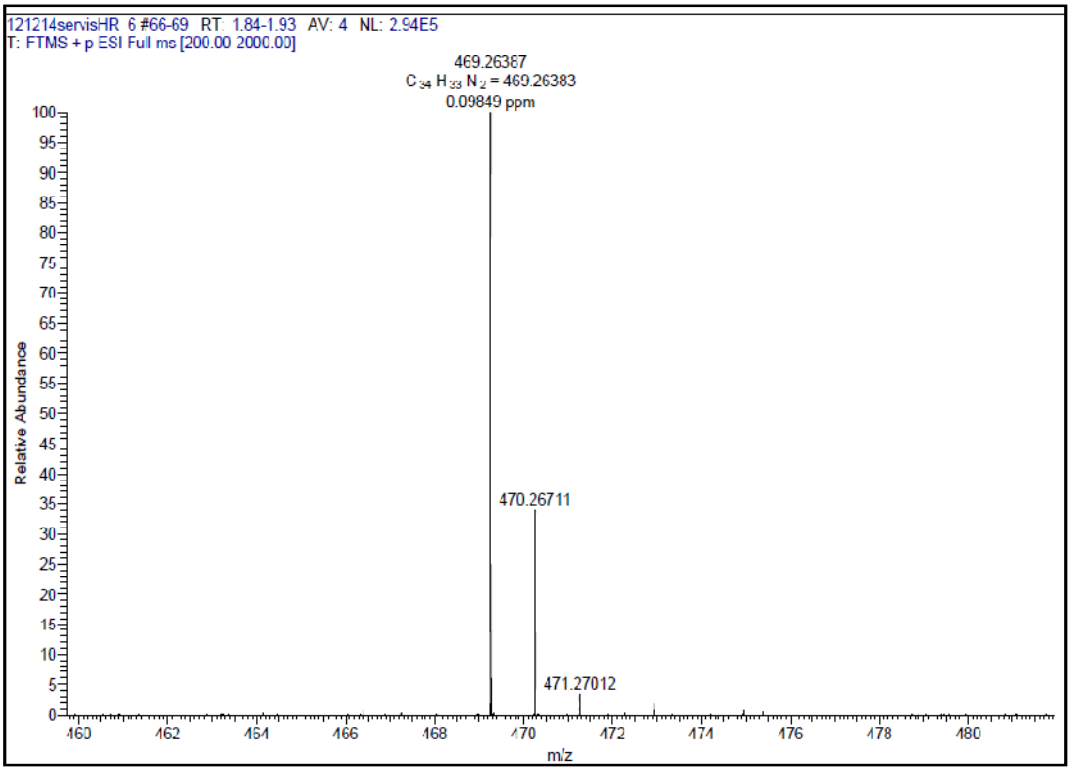
EI mass of (S)-methyl 1-(2-(9H-fluoren-4-yl)benzyl)pyrrolidine-2-carboxylate (25)



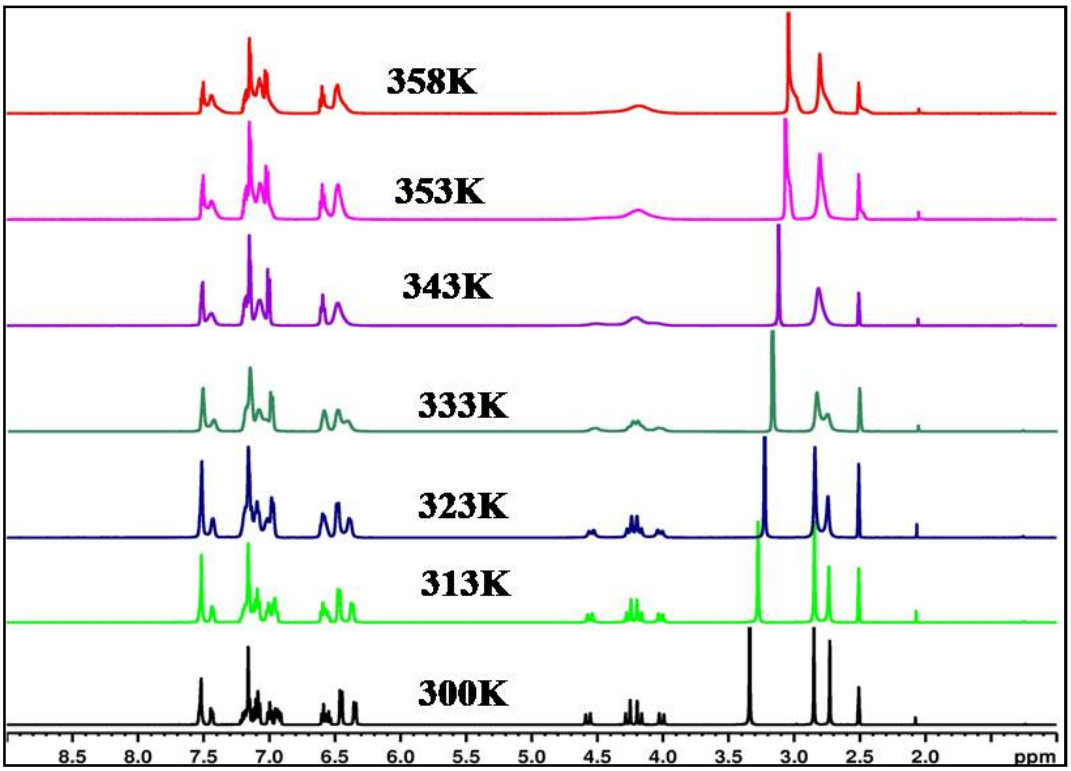
^{1}H-NMR spectrum of N,N'-([1,1':2',1''-terphenyl]-2,2''-diylbis(methylene))bis(N-methylaniline) (31) in $CDCl_3$ on 400 MHz



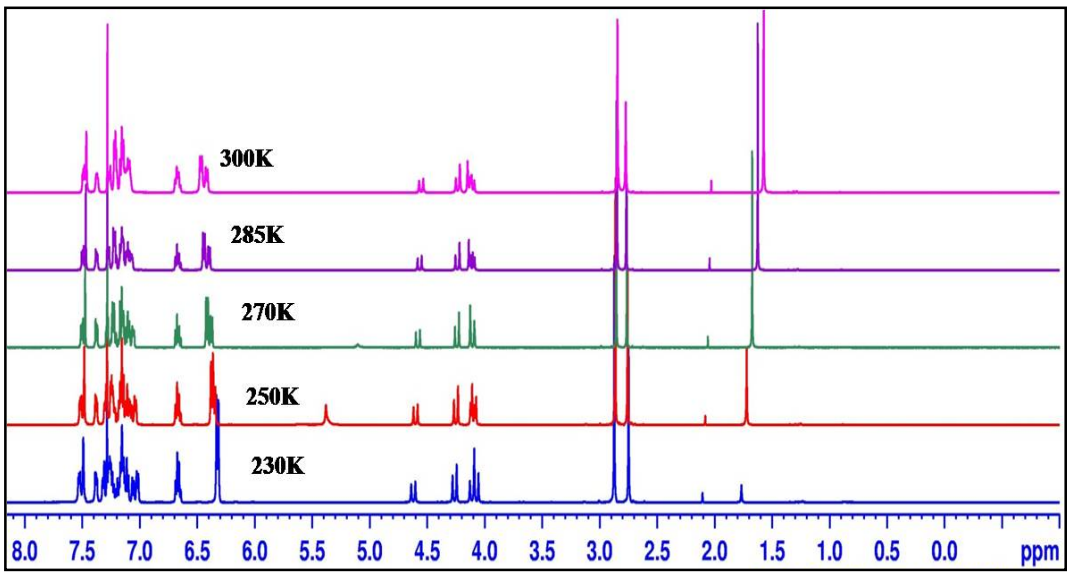
^{13}C-NMR spectrum of N,N'-([1,1':2',1''-terphenyl]-2,2''-diylbis(methylene))bis(N-methylaniline) (31) in $CDCl_3$ on 100.6 MHz



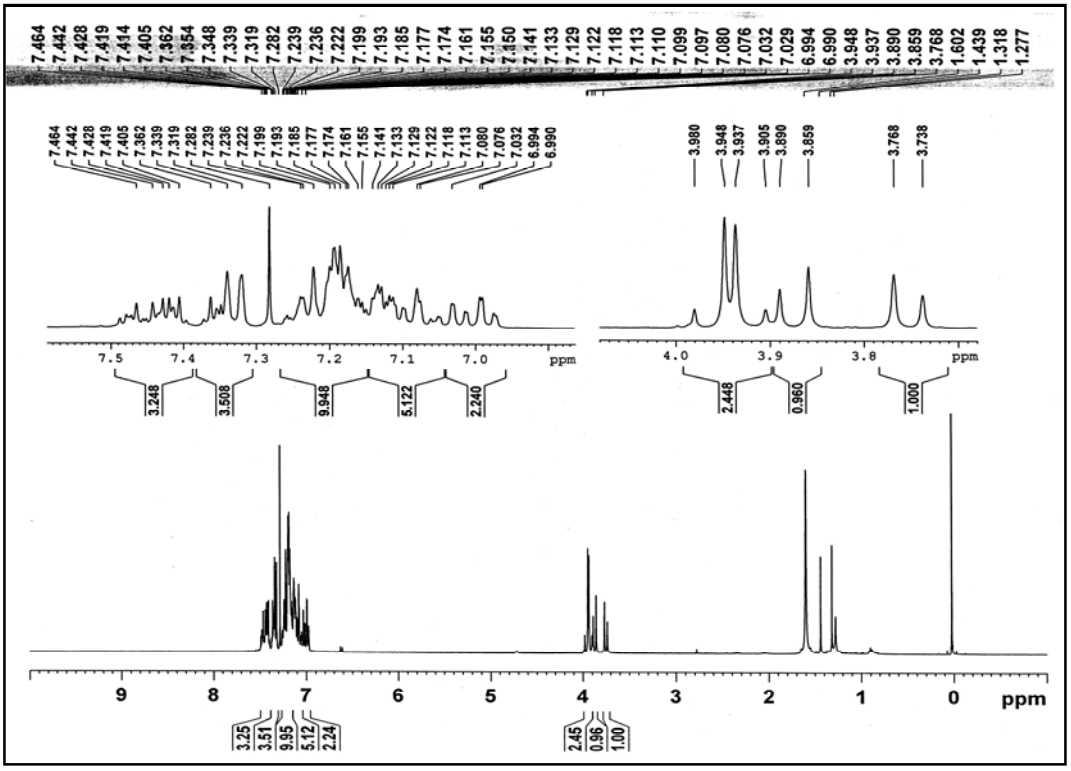
HRMS of compound N,N'-([1,1':2',1''-terphenyl]-2,2''-diylbis(methylene))bis(N-methylaniline) (31)



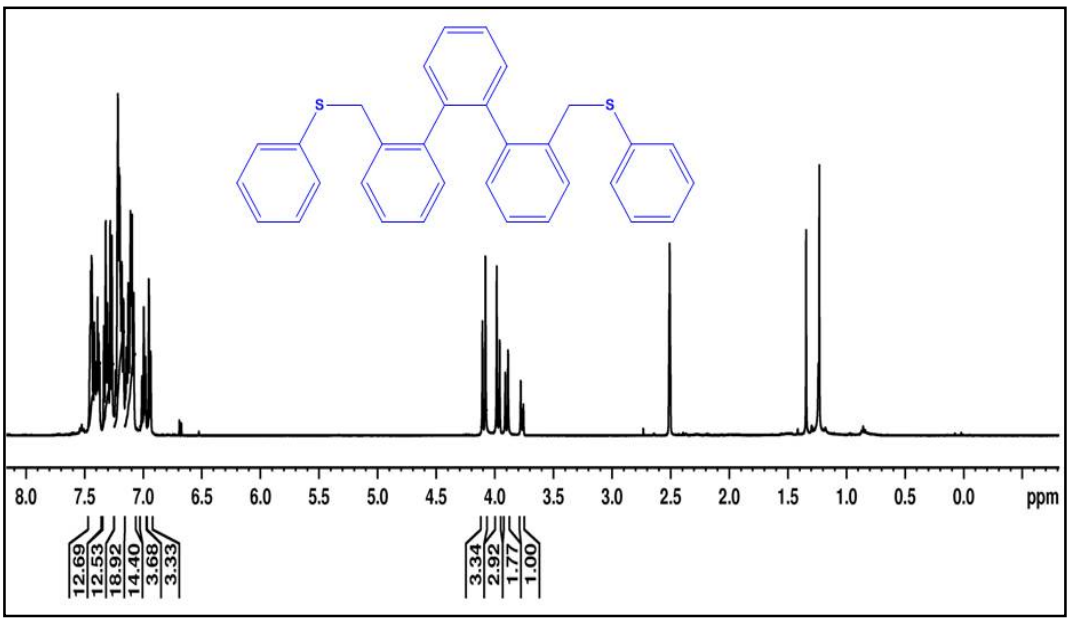
^{1}H-NMR spectrum of compound N,N'-([1,1':2',1''-terphenyl]-2,2''-diylbis(methylene))bis(N-methylaniline) (31) at different temperature (500MHz, DMSO-d_6)



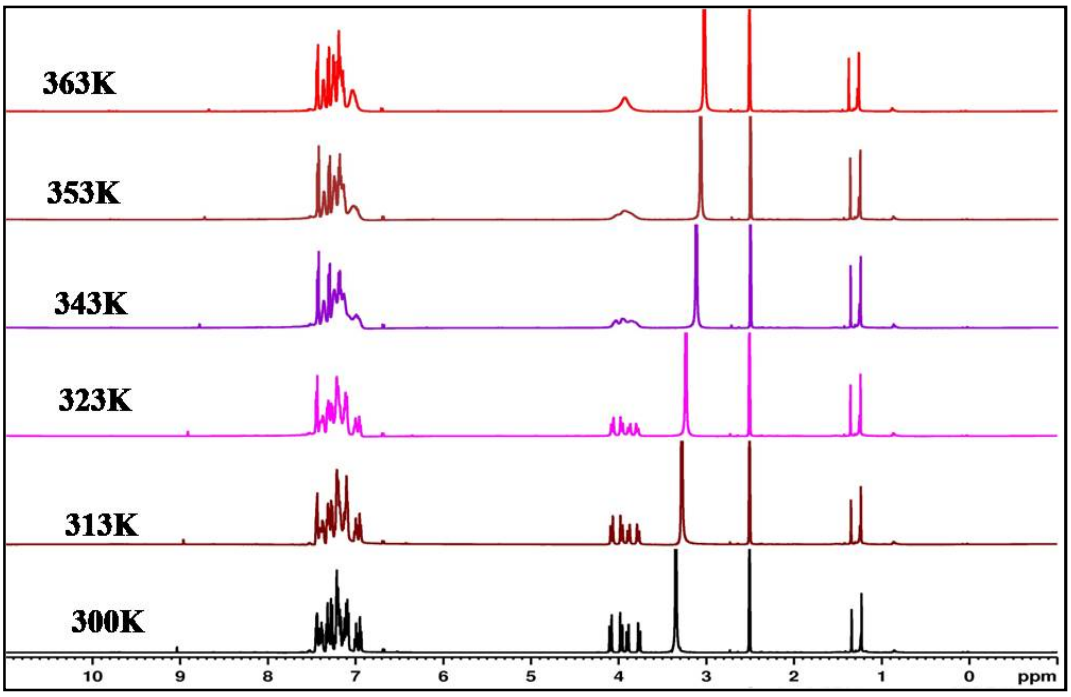
^{1}H-NMR spectrum of compound N,N'-([1,1':2',1''-terphenyl]-2,2''-diylbis(methylene))bis(N-methylaniline) (31) at different temperature (low temperature) (500MHz, DMSO-d_6)



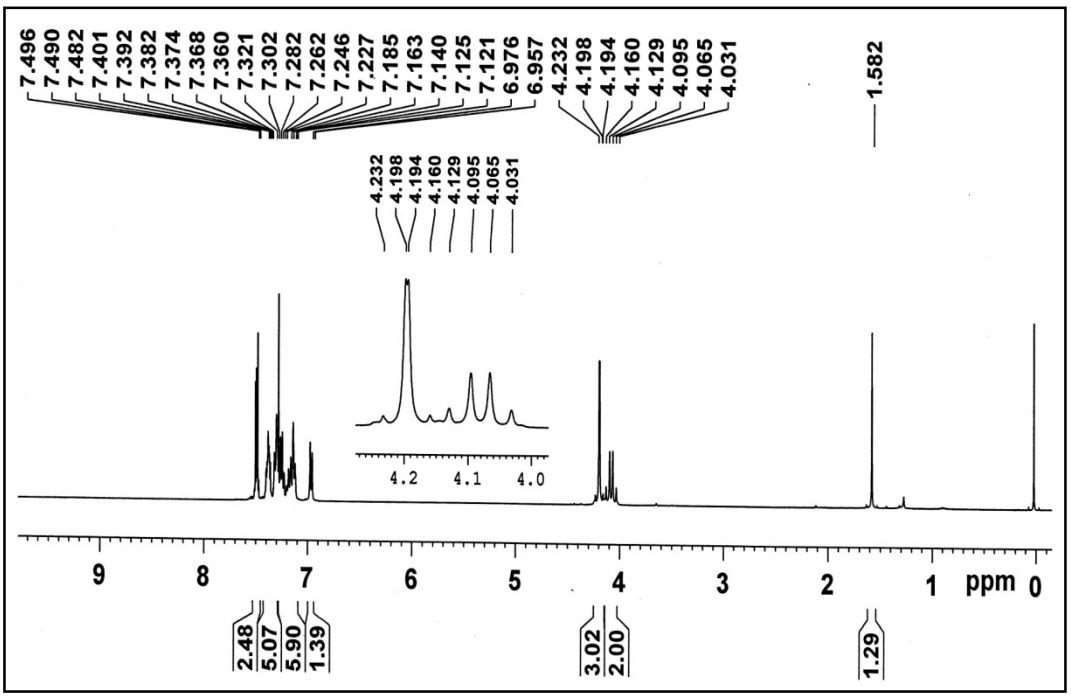
^{1}H-NMR spectrum of 2,2''-bis((phenylthio)methyl)-1,1':2',1''-terphenyl (33) in $CDCl_3$ on 400 MHz



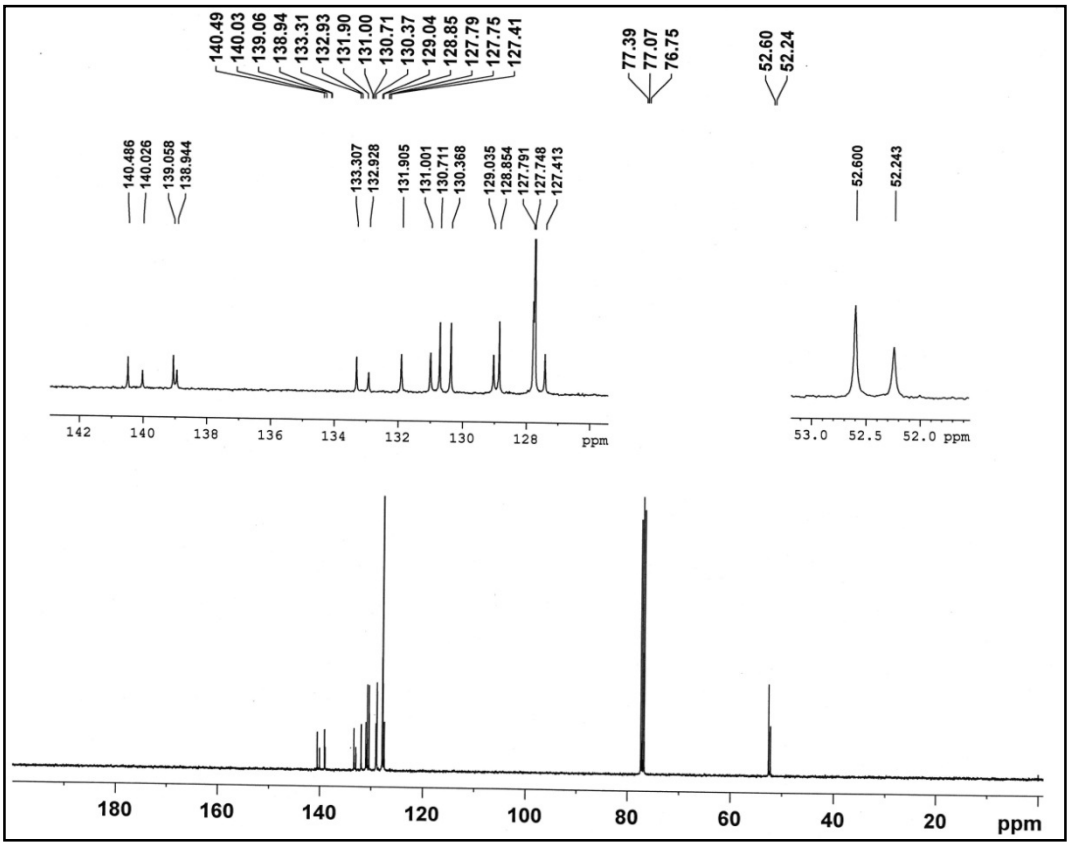
^{1}H-NMR spectrum of 2,2''-bis((phenylthio)methyl)-1,1':2',1''-terphenyl (33) (500 MHz, DMSO-d_6)



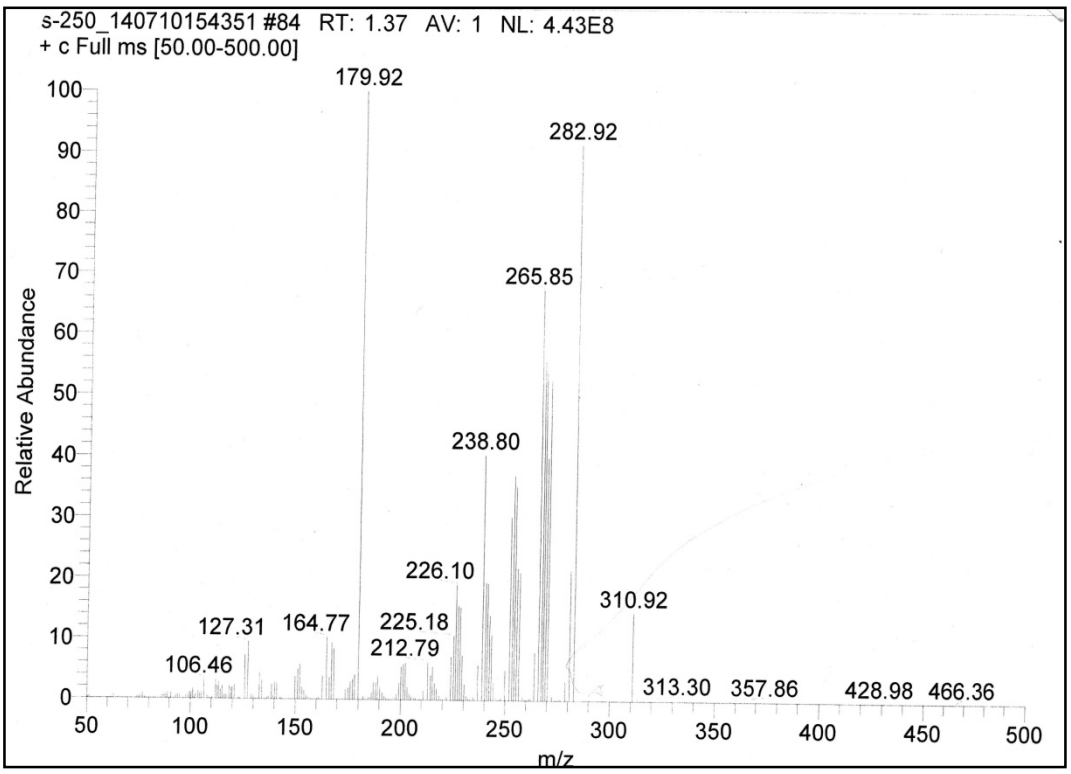
^{1}H-NMR spectrum of compound 2,2''-bis((phenylthio)methyl)-1,1':2',1''-terphenyl (33) at different temperature (500MHz, DMSO-d_6)



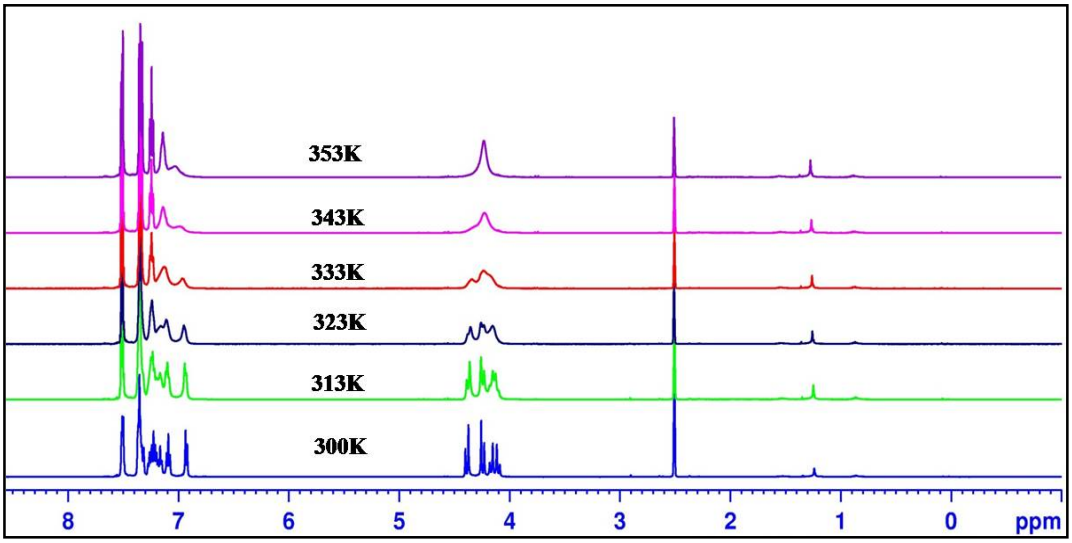
^{1}H-NMR spectrum of 2,2''-bis(azidomethyl)-*o*-terphenyl (34) in $CDCl_3$ on 400 MHz



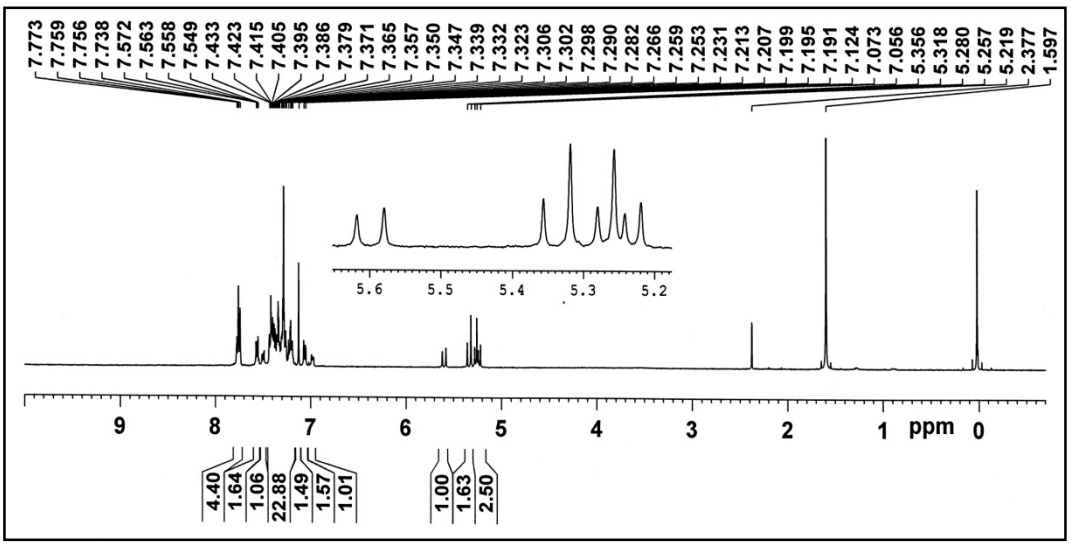
^{13}C-NMR spectrum of 2,2''-bis(azidomethyl)-*o*-terphenyl (34) in $CDCl_3$ on 100.6 MHz



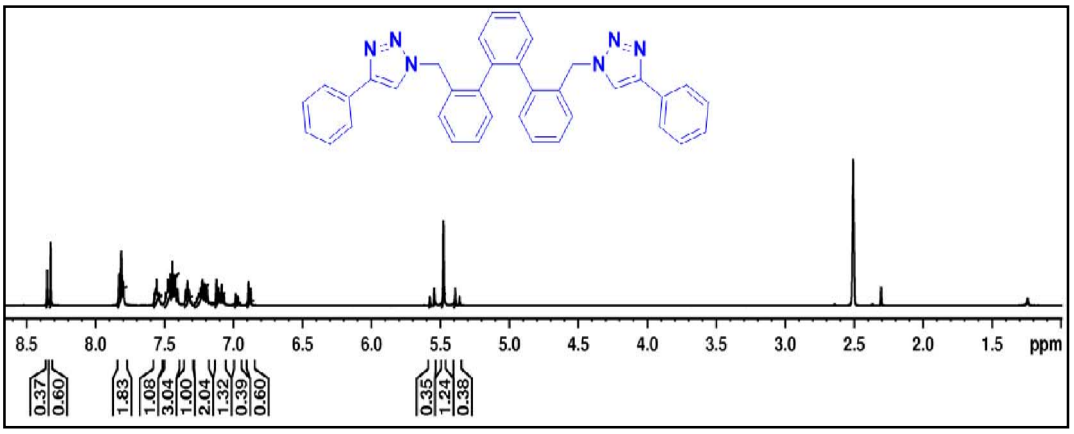
EI mass of 2,2''-bis(azidomethyl)-*o*-terphenyl (34)



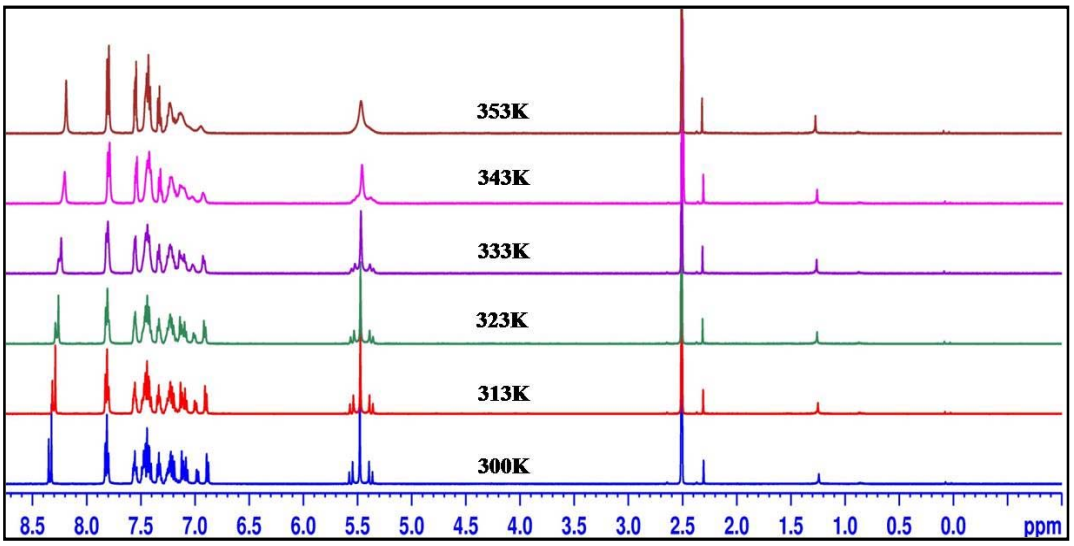
^{1}H NMR spectrum of compound 2,2''-bis(azidomethyl)-*o*-terphenyl (34) at different temperature (500MHz, DMSO-d_6)



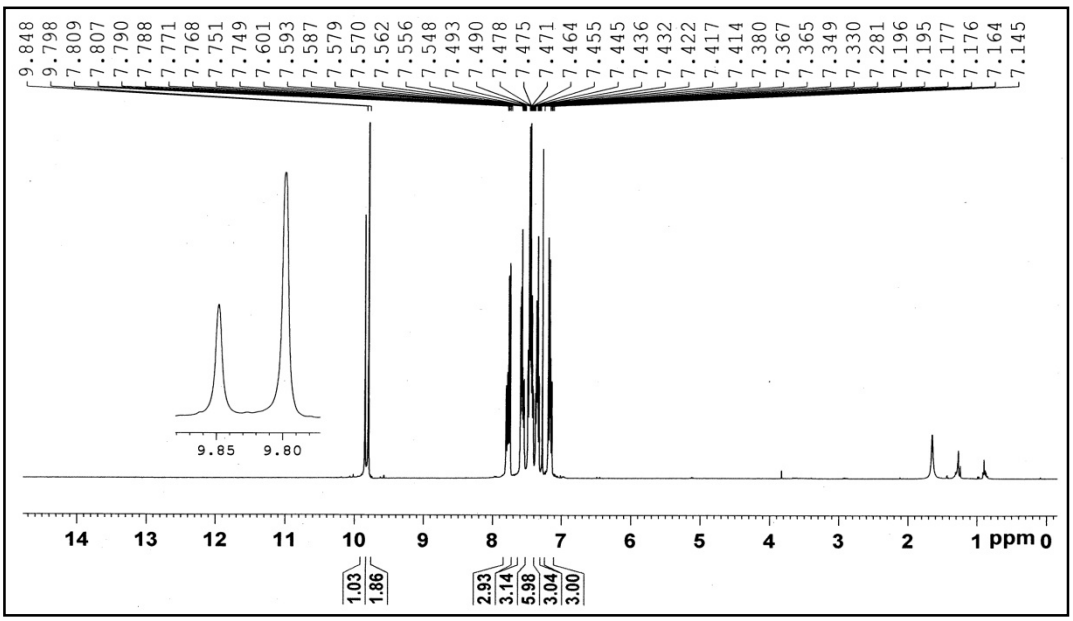
^{1}H-NMR spectrum of 2,2''-bis((4-phenyl-1H-1,2,3-triazol-1-yl)methyl)-*o*-terphenyl (36) in $CDCl_3$ on 400 MHz



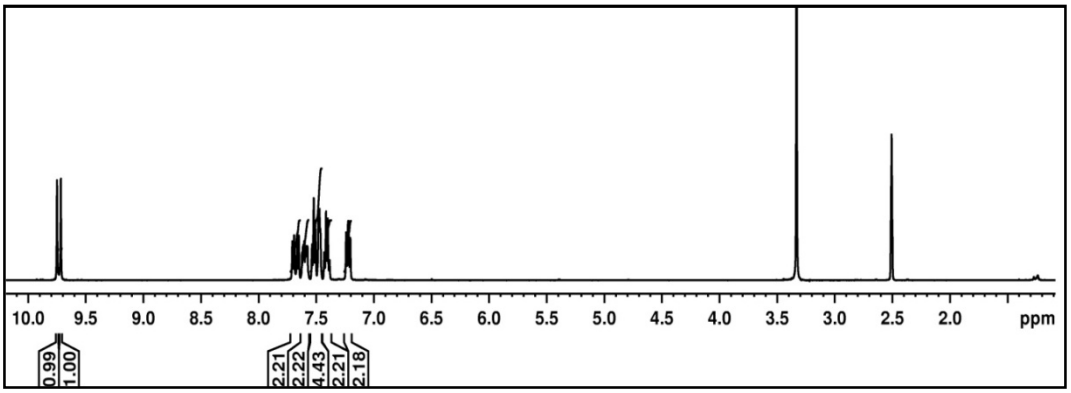
^{1}H-NMR spectrum of 2,2''-bis((4-phenyl-1H-1,2,3-triazol-1-yl)methyl)-*o*-terphenyl 36 (500 MHz, DMSO-d_6, 300 K)



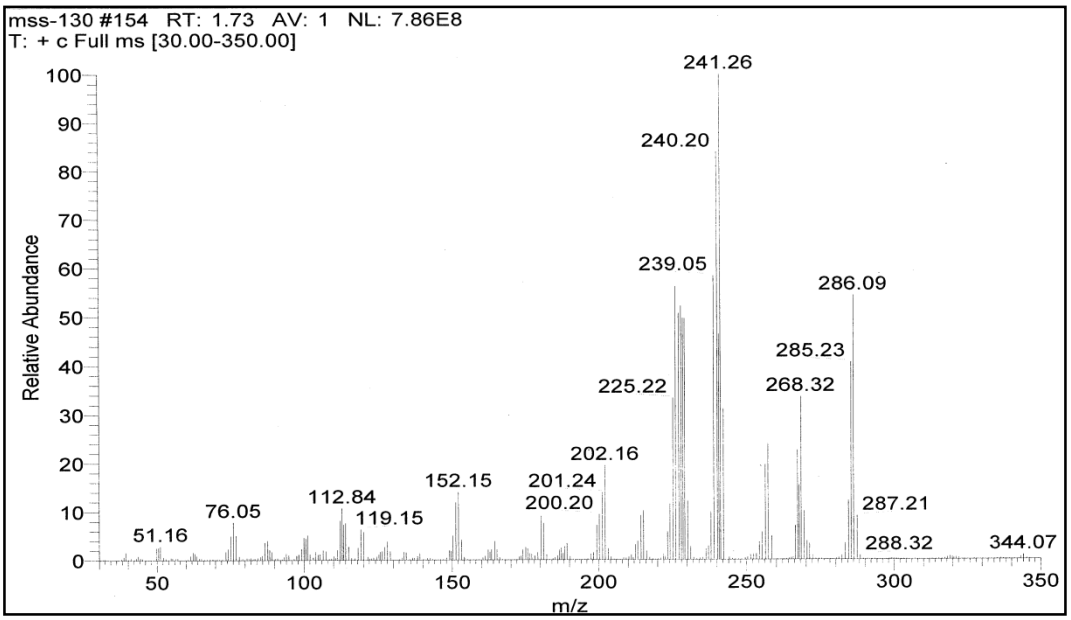
^{1}H-NMR spectrum of compound 2,2''-bis((4-phenyl-1H-1,2,3-triazol-1-yl)methyl)-*o*-terphenyl (36) at different temperature (500MHz, DMSO-d_6)



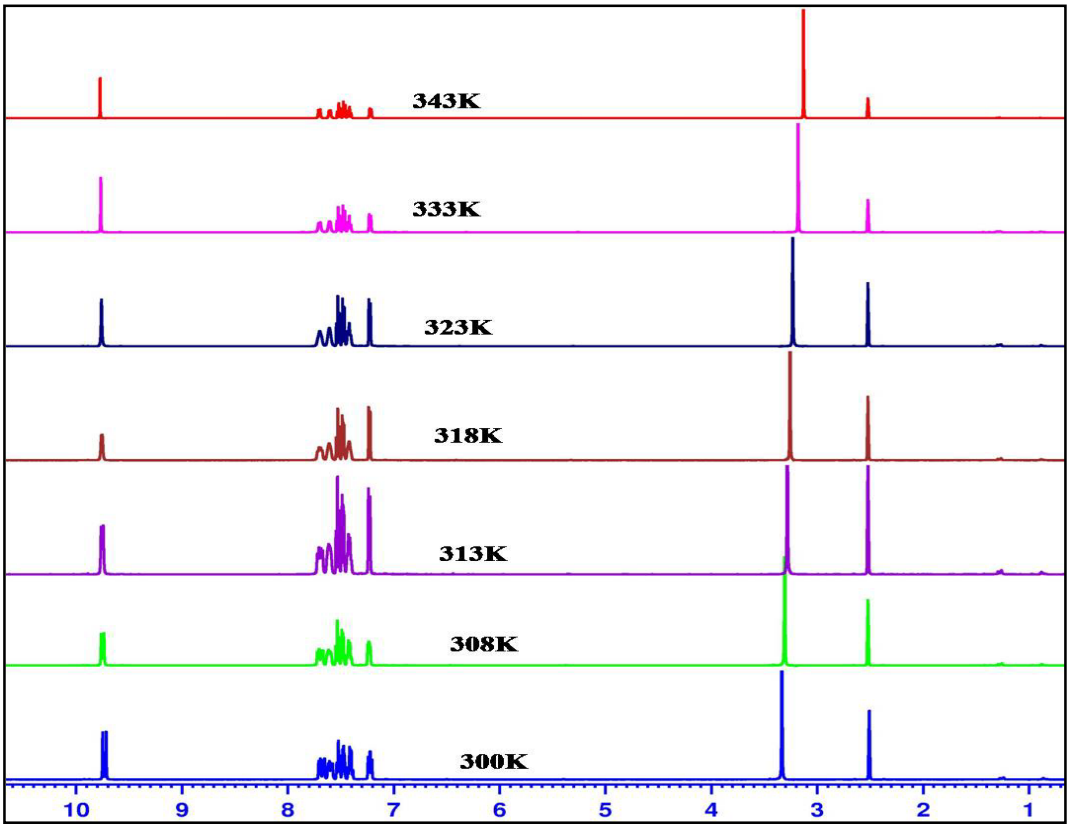
^{1}H-NMR spectrum of 2,2''-dicarbaldehyde-*o*-terphenyl (37) in $CDCl_3$ on 400 MHz



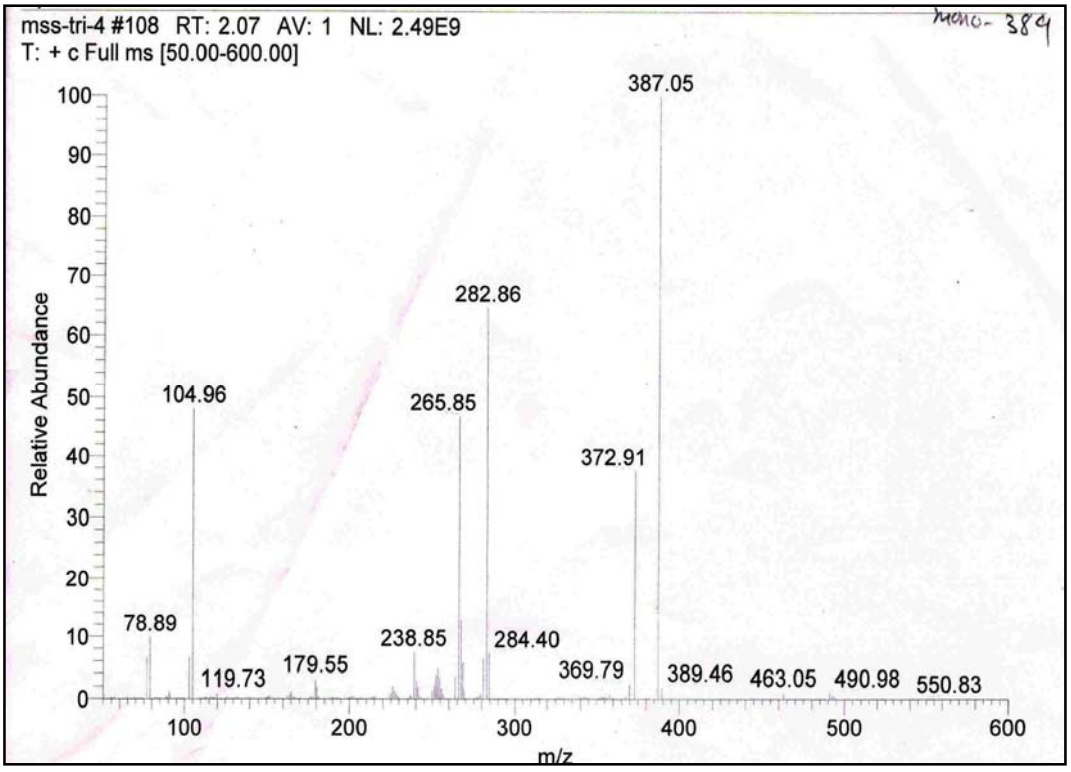
^{1}HNMR spectrum of 2,2''-dicarbaldehyde-*o*-terphenyl (37) (500 MHz, DMSO-d_6, 300 K)



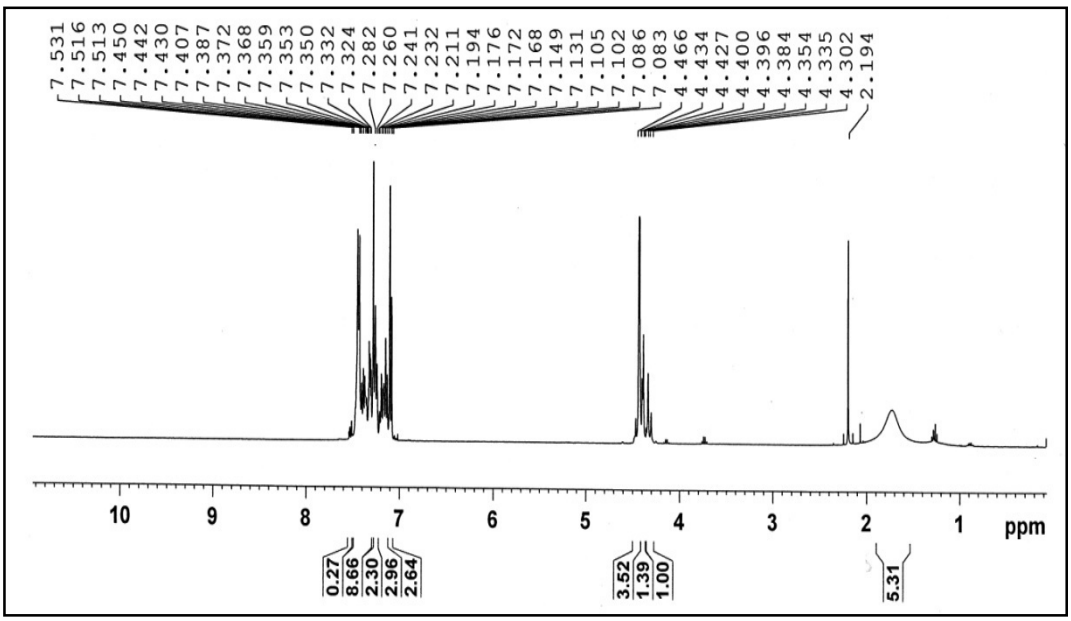
EI mass of 2,2''-dicarbaldehyde-*o*-terphenyl (37)



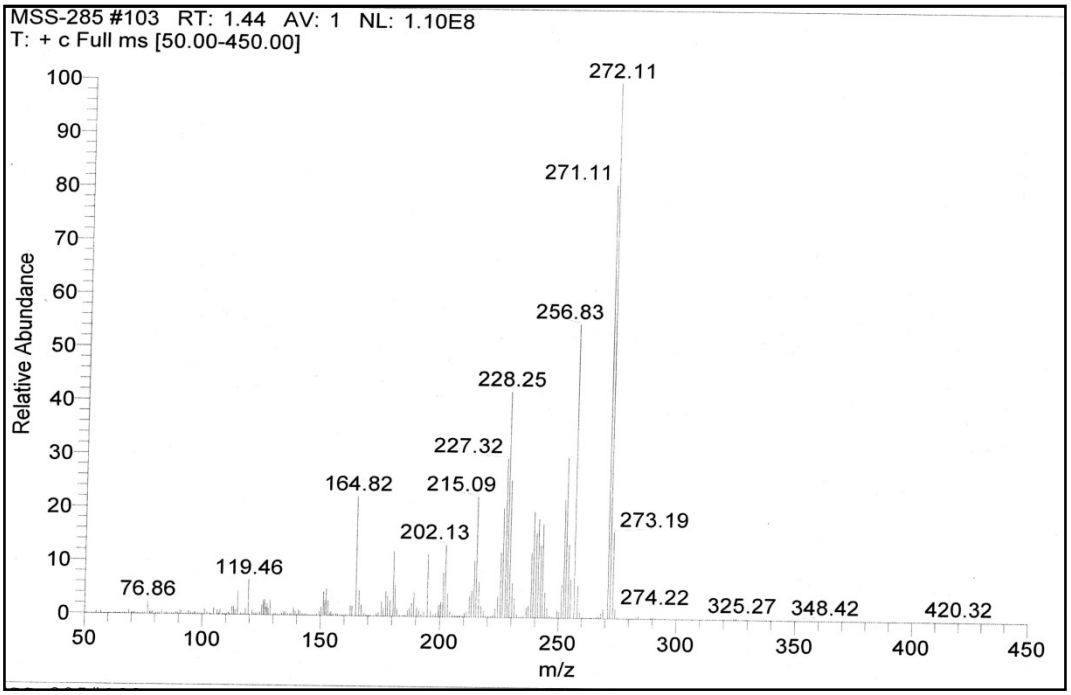
^{1}H-NMR spectrum of compound 2,2''-dicarbaldehyde-*o*-terphenyl (37) at different temperature (500MHz, DMSO-d_6)



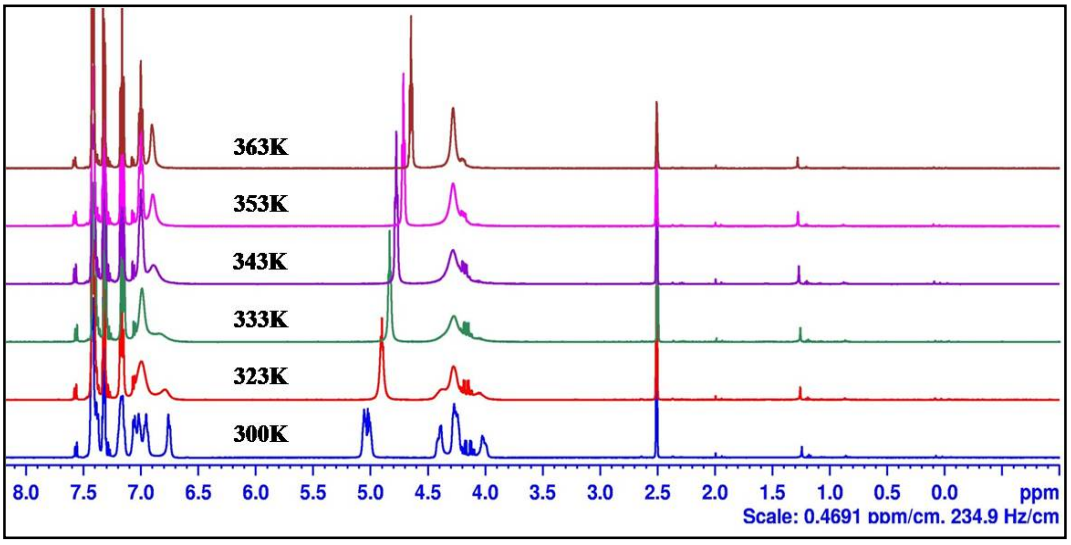
EI mass of *ortho*-terphenyl-2,2''-diyldimethanol (38)



^{1}H-NMR spectrum of *ortho*-terphenyl-2,2''-diyldimethanol (39) in $CDCl_3$ on 400 MHz

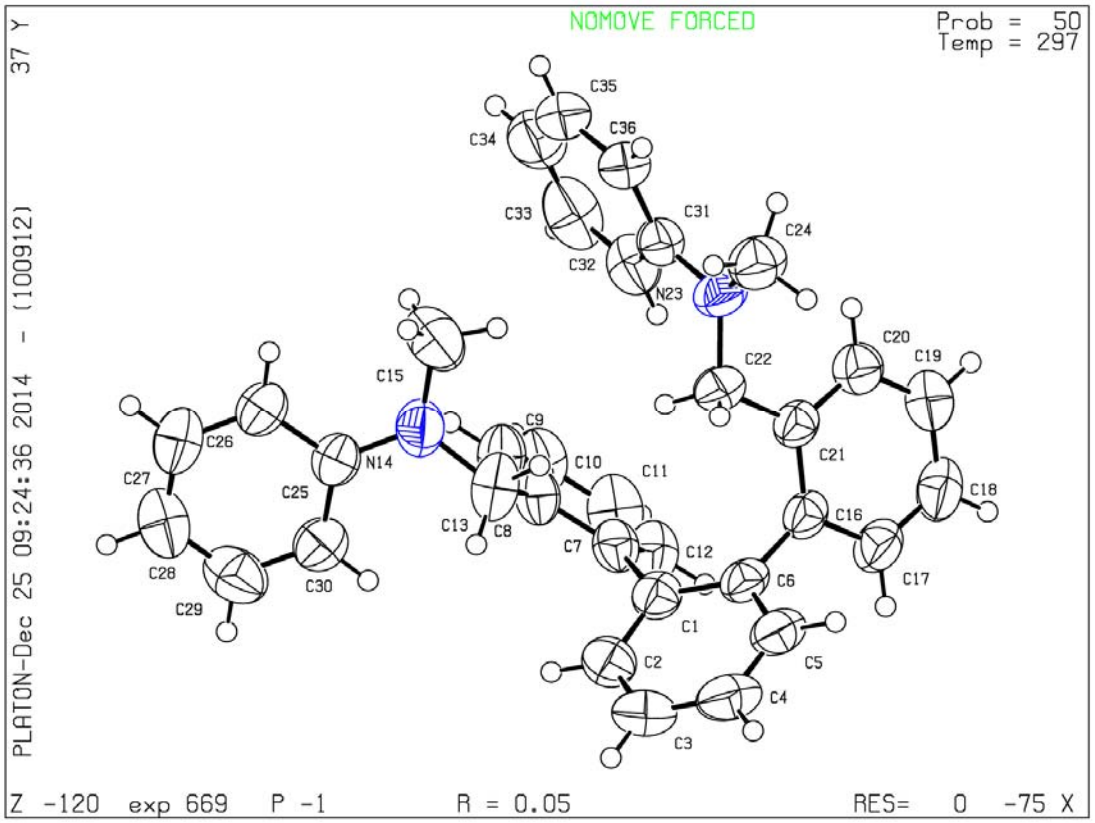


EI mass of *ortho*-terphenyl-2,2''-diyldimethanol (39)



^{1}H NMR spectrum of compound *ortho*-terphenyl-2,2''-diyldimethanol (39) at different temperature (500MHz, DMSO-d_6)

X-ray data for compound 31 (CCDC 1424142)



ORTEP diagram of **31** with atom numbering scheme 50% probability factor for the thermal ellipsoids.

Crystal data and structure refinement for compound 31.

Empirical formula	$C_{34}H_{32}N_2$
Formula weight	468.62
Temperature/K	297
Crystal system	triclinic
Space group	P-1
a/Å	9.6948(4)
b/Å	10.7610(5)
c/Å	13.0648(5)
α/°	80.500(3)
β/°	79.104(3)
γ/°	81.145(4)
Volume/Å^3	1309.42(10)
Z	2
ρ_{calc}g/cm^3	1.1885
μ/mm^{-1}	0.523
F(000)	500.0
Radiation	Cu Kα (λ = 1.54184)
2Θ range for data collection/°	9.36 to 142.62
Index ranges	$-11 \leq h \leq 11$, $-13 \leq k \leq 13$, $-15 \leq l \leq 12$
Reflections collected	6884
Independent reflections	5079 [R_{int} = 0.0107, R_{sigma} = 0.0194]
Data/restraints/parameters	5079/0/327
Goodness-of-fit on F^2	1.086
Final R indexes [I>=2σ (I)]	R_1 = 0.0462, wR_2 = 0.1270
Final R indexes [all data]	R_1 = 0.0500, wR_2 = 0.1320
Largest diff. peak/hole / e Å^{-3}	0.16/-0.15

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